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The Terminology of the Rh Blood Group System

'Let us . . . confound their language, that they may not understand one another's speech'. (Genesis, 11, *The Tower of Babel*).

By 1940 it had become clear from the observations of Landsteiner and Wiener and of Levine that an important new blood group system had been established. The general name Rh which was applied was derived from 'Rhesus', because it was with the red blood cells of this type of monkey that an antiserum was prepared in rabbits which made possible the detection of this new property of the human red blood cell. The epochal quality of the discovery of this new blood group system is of Nobel prize stature.

Apart from the implications of this work for clinical medicine, anthropology and genetics, the forensic applications are clearly also of the greatest importance. The rapid increase in our knowledge of the Rh blood group system, when added to that of the other known blood group systems, makes it possible to exclude about 62% of men wrongfully accused of paternity.[1]

Since evidence based on Rh testing is now offered in courts all over the world, the need for a standardized, universally acceptable nomenclature has become essential. Indeed, there is an inescapable duty on workers in this field to agree on such a terminology, if they are to avoid confusion in the courts and possible discredit of much entirely valid work applicable to medico-legal problems. A fundamentally similar situation existed before World War I in the ABO blood group system. The League of Nations Committee which went into the matter had to consider 5 different nomenclatures current at that time, but it was nevertheless not beyond the wit of man to adopt a uniform terminology which has stood the test of time.

1. Race, R. R. and Sanger, R. (1954): *Blood Groups in Man*, 2nd ed., p. 344. Oxford: Blackwell Scientific Publications.

In both the ABO and MN systems there is now world-wide agreement about the terminology, the materials used for testing and the way in which results obtained are designated. The deductions made are positively determined and not derived by devious and indirect inferences. The terminology identifies a blood without attempting to describe every serological property of that blood, known or yet to be discovered.

In the Rh system, however, there is not general agreement about the nomenclature, the dissension being mainly between Wiener's (Rh-Hr) International Nomenclature and that of British workers typified in the Fisher-Race usage which employs an alphabetical (CcDdEeFf) pattern.

The Fisher-Race terminology is based on an hypothesis of closely linked genes which admits the possibility of the genetic mechanism of crossing-over in the chromosomes, even though no single example of this has yet been demonstrated. Moreover, the terminology favoured by British authors does not always describe an Rh blood type as a positive, direct deduction from the tests actually performed in the laboratory. The Rh-negative blood designated rh by Wiener is referred to as *cde* by Race and Sanger. Wiener's description rh connotes that such a blood reacts negatively with certain antisera (anti-**rh′**, anti-$\mathbf{Rh_0}$ and anti-**rh″**). In the opposing nomenclature this blood is called *cde* not because it reacts positively with anti-*c*, anti-*d* and anti-*e* sera, but because it fails to react with anti-*C*, anti-*D* and anti-*E* sera. There is an assumption that failure to react with anti-*C*, anti-*D* and anti-*E* implies a positive reaction with the reciprocal antisera anti-*c*, anti-*d* and anti-*e*. In fact, anti-*d* has never definitely been proved to exist and anti-*c* and anti-*e* are rare antisera not generally available and therefore seldom, if ever, employed in practice for the identification of the Rh-negative type.

The example of the Rh-negative type (rh or *cde*) typifies the fundamental nature of the nomenclatural conflict in this field. The courts are concerned with facts and not fancies, whether the latter concern the existence of postulated (and unproven) reciprocal antisera or multiple closely linked loci on a chromosome. Any alleged designation of fact which invokes unproved and at present untestable hypotheses will be viewed with considerable hesitation in judicial circles. It would therefore be more desirable to *identify* Rh blood types (phenotypes) in a language which is a factual recognition of the blood type, without forcing on the expert a terminology which aims to identify it by *describing* every actual and hypothetical property of that blood. This has been achieved in the ABO and MN systems of nomenclature and appears possible in the Rh system with Wiener's terminology.

The acceptability of evidence regarding paternity based on Rh blood tests depends on the fact that certain properties of the blood are inherited in a constant fashion without exception. From this it follows that certain blood types cannot result from certain matings. The identity of a blood

type should therefore be conveyed unequivocally. It should not be done in terms of hypothetical properties some of which have not been proved to exist. Most authoritative texts which employ the CDE system also use Wiener's terminology or a palpably obvious modification, thereby tacitly admitting the shortcomings of the CDE system of description.

Elsewhere in this issue (p. 236) Wiener demonstrates the confusion which can arise in the interpretation of paternity tests as a result of this hybrid bilingualism. If we are to avoid the construction of a modern tower of Babel in this important field, it is essential for early agreement on a standardized nomenclature. Wiener has made out a powerful and cogent case for the international adoption of his terminology. The fact that it involves an unfamiliar symbolism which may be difficult for the dilettante or the amateur is not an adequate reason for opposing it. The terminology of statistics, nuclear physics and many other scientific disciplines is not determined by the ease with which the uninformed will be able to appreciate it. By the same token, it would be irrational to demand of the Rh terminology an alphabetical simplicity because it is best suited to those equipped with only a modest literacy in this field.

Wiener's article in this issue also makes clear the complexity and intricacy which has developed in the study of the Rh system. The performance of Rh tests and the expression of an opinion on the results has now become the province of the expert with special training in, and practical experience and a comprehensive understanding of these problems. Both legal and medical practitioners should recognize that in medico-legal disputes involving Rh testing, it is now necessary to consult such specially qualified experts.

* * * *

British Association of Forensic Pathologists

The Eleventh Meeting was arranged at St. George's Hospital, London, on Saturday 19 November 1955. The main item scheduled for discussion in the morning session was a symposium on *Alcohol in Forensic Problems.* Participants: Dr. W. R. Heddy, Dr. J. Imrie and Dr. J. A. Hobson.

The afternoon session provided for a discussion on the policy of the Association and amendments to its Rules (opened by Prof. J. Glaister) as well as a Business Meeting of Fellows and short papers contributed by Members and Associate Members.

An Investigation of Cases of Arsenical Poisoning†

P. R. v. d. R. Copeman, B.A., D.Sc.*

and

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Division of Chemical Services, Johannesburg

Few poisons have exercised so popular an appeal as arsenic in one or other of its forms and, at the same time, involved so many problems. The element is widely distributed in nature and its toxic properties have been known throughout the ages. The poisoners of the Middle Ages employed it extensively and, until the middle of the 19th century, it was the most commonly used poison. It was a common ingredient in many of the secret potions brewed for the purpose of removing unwanted rivals. Its popularity, in Europe at least, has declined owing partly to the knowledge that its presence can be established easily in viscera, even after a long period of burial. It is an elemental substance which is not destroyed during the processes of decomposition of the body and therefore persists as a record of the past. Consideration such as these caused many a poisoner to turn to 'safer' and less easily detected poisons.

In South Africa arsenic still occupies a prominent position in the list of poisons used, probably because a more intimate knowledge of its properties is not so widespread and also because it is relatively easily obtainable in the form, e.g. of arsenical dips and pest remedies. The lack of knowledge of the properties of arsenic in South Africa is understandable in the light of the preponderance of a more primitive Native population. It is interesting to note that, during the period 1948–1952, 22% of the number of deaths from arsenical poisoning were European and the remainder were Native and 'mixed'. This is more or less in the same proportion as that for the two main races in South Africa. It would appear that arsenic, which may be regarded as a poison of European origin, is preferred by the Native to many of his own poisons when murder is contemplated.

The introduction of the newer organic insecticides, such as D.D.T., B.H.C., Thiophos, etc. had led to a *relative* decrease in the number of deaths from

† This paper deals with the examination of the results obtained in cases of arsenical poisoning during the period 1948 to 1952 and is an extension and amplification of the article published by Copeman and Kamerman in 1940.[1]

* Chief Professional Officer.

‡ Principal Professional Officer.

arsenical poisoning. These poisons have, however, introduced greater complications in the matter of detection. During the period 1932–1940, the proportion of deaths from arsenical poisoning was 46% of the total positive cases while in 1948–1952 this proportion was 27%. During the former period, however, the average number of deaths from this cause was only 16 per annum while during the latter period it was 23 per annum. These figures indicate the great increase in the number of cases investigated during recent years. It must be remembered that a substance with emetic or purgative properties has an irresistible attraction for the Native mind and arsenic is pre-eminently a substance of this class. It is thus quite possible that death from arsenical poisoning may have occurred more from ignorance of the dangers involved than from its conscious use as a poison. The use of ant poison, containing arsenic, for suicidal purposes appears to be common among Europeans. Of 15 suicides by Europeans from arsenical poisoning 13 were due to the use of 'ant poison'. This is probably due to the fact that ant poison is a common household preparation. However, as long as such preparations are readily available to the public, it is likely that arsenic will continue to occupy a leading place among South African poisons.

Methods of Investigation

In cases of suspected poisoning, specimens of the viscera, usually the liver, kidneys and stomach, are submitted to the Government Chemical Laboratories, Johannesburg, for toxicological examination. A portion is always, as a matter of routine, subject to the Reinsch test for arsenic. If the presence of arsenic is established by this test, aliquot weights of the finely divided organs are digested with a mixture of sulphuric and nitric acids to destroy the organic matter. When oxidation is complete all traces of nitric acid are removed and the arsenic in the solution usually determined by Green's method.[3] When the amounts of arsenic present are very small, a modified form of this method is used for the determination. When extremely small amounts have to be detected qualitatively or determined with a modicum of accuracy, as in the case of soils, the Gutzeit method may be used employing paper discs, as this has been found sufficiently sensitive for all practical purposes.

Distribution of Arsenic in the Body

Arsenic is not a cumulative poison in the true sense of the word, since it is eliminated fairly rapidly from the system. Elimination of arsenic may occur through the urine, the faeces, the epidermal tissues and, to some extent, through the sweat, the relative amounts varying with the conditions of absorption from the gastro-intestinal tract. The distribution of the arsenic in the body will depend greatly upon the interval between the taking of the toxic dose and the death of the individual. In rapidly fatal cases the stomach may show relatively larger amounts of arsenic than the other organs as there may not have been sufficient time for much of the poison to be absorbed. However, if vomiting has been excessive, a large part of the

ingested arsenic may be lost. During the earlier stages of poisoning, an accumulation of arsenic tends to occur in the liver and in the kidneys but, if the victim manages to survive for a few days, the amount in the liver gradually decreases until, finally, the concentration of arsenic reaches what must be regarded as the normal content of the tissues. However, since the rate of elimination decreases as the amount of accumulated arsenic decreases, the normal level may not be reached for some considerable time. Such elimination may take place through the urine, but the absence of arsenic from any one sample of urine is no proof that elimination is complete since elimination of arsenic through the urine is intermittent. In cases of acute poisoning the urine ceases to show the presence of arsenic in about 10 days, though the liver may still contain arsenic. In chronic cases as reported by Webster[6] and Winter Blyth[7] arsenic may continue to be eliminated from the system in this way for two or three months, owing to the more widespread accumulation of arsenic in all tissues.

Another channel of elimination of arsenic from the system is through the keratin tissues, such as the skin, hair, nails and, in cases of chronic poisoning, these tissues, especially the hair, are of great assistance in establishing the possibility of chronic arsenical poisoning. As will be explained later, in cases of acute poisoning, the analysis of hair and nails for arsenic has no value. Sydney Smith[5] has shown, however, that the greatest care must be taken to avoid contamination of hair and nails by any of the body fluids since arsenic is readily absorbed from solution by keratin tissue.

Normal Arsenic Content of Tissues

Although arsenic is not a natural constituent of the body and, as far as is known, plays no essential part in natural biological processes, the presence of traces of arsenic in foodstuffs, chemicals, etc. leads to the presence of small amounts in the various organs and tissues. In Table I the amounts normally found in the human system under South African conditions are given in terms of parts per million (p.p.m.) or milligrams per kilogram. These figures have been obtained from a large number of analyses and showed very little variation in the amounts normally found in viscera.

For the sake of comparison the results are also given for 2 cases, one of chronic arsenical poisoning and one of death after an arsenical injection

Table I: Amounts of Arsenious Oxide in Organs

Material	*'Normal'*	*Chronic*	*Injection*
Liver	0·2—0·4	0·8	1·2
Kidneys	0·2—0·4	—	1·8
Bones	0·2	—	—
Blood	0·2—0·4	—	—
Hair	3—5	30·0	—
Nails	3—5	—	—
Urine	0·15	—	—

for venereal disease. In the first case the patient was in hospital for 3 weeks before death, but there was a history of chronic arsenical poisoning. The case for chronic poisoning is borne out by the high arsenical content of the hair.

It is clear, therefore, that, owing to the presence of small amounts of arsenic normally in the system, it is necessary to be careful in assigning a significance to any small amounts which may be found in the viscera, to allow a fair margin of safety, and to take the previous history of any case into account before accepting any low figures as indicating arsenical poisoning. This is particularly true in cases of chronic poisoning but, in general, there is usually a wide gap between the amounts found in such cases and the amounts normally present. The importance of determining the arsenical content of the hair and, if possible, the nails, is clearly evident and cannot be overstressed.

Accumulation of Arsenic in the System

In regard to the accumulation of arsenic in the liver there does not appear to be any fixed maximum limit to the amount which can be absorbed and this may vary within wide limits. Webster[6] has reported amounts up to 700 mg.* and in a previous paper[1] two cases were reported where 715 mg. and 750 mg. had been recovered from the liver. During the period 1948–1952, an exceptional case (No. 8260/49) was investigated in which 1,332 mg. were recovered from the liver alone. This was a case of suicide by a European female adult and the liver, kidneys, stomach and contents as well as intestines and contents were submitted for analysis. A total amount of 11.3 gm. arsenious oxide was recovered from the organs submitted. Two exhibits were forwarded, one, a sample of arsenious oxide and the other, a sample of weed-killer, consisting of a solution of sodium arsenite containing 38.4% of arsenious oxide. There was no history of vomiting or purging and unfortunately no information was available concerning the time between ingestion and death. On the assumption that no arsenic was eliminated from the system, the deceased must have drunk at least a fluid ounce of the weed killer.

This was an exceptional case. The average amount of arsenic in the liver for 72 cases, excluding those involving children, was found to be 75 mg. In the kidneys the average amount was found to be 11.5 mg. with a range of 0.1 mg. to 169.0 mg. of arsenious oxide. The amounts found in these organs will, of course, depend upon many factors, such as the amount taken, the form in which it was taken, the time elapsing before death, etc. If arsenic is taken in actual solution, absorption probably begins immediately. The liver and kidneys retain appreciable amounts of arsenic but some of the absorbed arsenic will be excreted rapidly by the kidneys.

* 65 mg. = 1 grain.

The amounts found in the stomach are subject to so many adventitious factors that no figures are given. Any factor affecting the rate of absorption from the gastro-intestinal tract will affect the amount remaining in the stomach and the intestines. Just how long a time must elapse before all the ingested arsenic will find its way out of the stomach, either by absorption or excretion, will depend upon the rapidity of absorption and the amount ingested. Any amounts actually found simply indicate that arsenic has been ingested before death. The variations are extremely wide. It is clear that, when considering the amounts of arsenic found in the various tissues, no definite rules can be formulated and each case must be treated on its own merits, due regard being had to all the circumstances and the history of the case and bearing in mind the results of previous experience.

Relation Between the Amounts of Arsenic Found and the Amounts Taken

Attempts have frequently been made to correlate the amounts found in organs such as the liver, the kidneys and the stomach with the amounts actually ingested. Owing to the inevitable lack of data concerning the amounts actually taken and of the amounts removed before death by such means as vomiting and purging, this problem seems incapable of solution. In addition, when it is considered that so many factors such as the age, health of the victim, fullness or emptiness of the stomach, severity of vomiting and/or purging and the time elapsing before death, influence the rate and amount of absorption, it is obvious that no clear-cut answer can be expected. In addition, the variability of a biological system such as that of the human being must be considered. In this connexion, the form of the arsenic and the method of administration have a direct bearing on the problem. For example, sodium arsenite is absorbed more rapidly than, say, arsenious sulphide or even 'white arsenic' (arsenious oxide). Arsenical compounds administered with solid or semi-solid foodstuffs, especially fatty foods, are less readily absorbed than those administered in fluids such as water.

Owing to the variations which occur not only in the absolute weights of the organs but in the relative weights of the liver and kidneys, it is somewhat difficult to compare the amounts of arsenic found in these organs in the different cases of arsenical poisoning. The variability of the data in this respect is clearly shown in Table II where the data, in terms of mg. per organ, have been grouped according to the time which has elapsed before death, where this is known.

It will be seen that the amounts in the organs tend to decrease with time and this is particularly noticeable in the stomach. The variations in the amounts in the liver are, however, so wide in any group that no definite conclusions can be drawn regarding the amounts that may have

Table II: Amounts of Arsenic in Organs

Case	*Liver (L)*	*Kidneys (K)*	*Stomach*	*Ratio L : K*	*Average*
A. Time of Death = Up to 3 Hours					
2801/52 ..	56·5	7·8	218·4	7·24	
2569/52 ..	193·7	9·1	13·6	21·29	
4994/52 ..	471·2	42·9	2109·2	10·98	
4905/50 ..	39·0	2·6	10·4	15·00	
4434/49 ..	15·6	5·2	44·8	3·00	
2232/49 ..	33·8	2·6	10·2	1·30	11·76
B. Time of Death = 4—24 Hours					
350/52 ..	29·9	1·9	16·9	15·74	
7015/52 ..	11·7	2·6	0·3	4·50	
4169/49 ..	55·9	2·6	5·2	21·50	
4367/48 ..	28·6	2·6	11·0	11·00	13·44
C. Time of Death = 5 Days or More					
6387/52 ..	11·0	0·6	—	18·33	
1536/51 ..	3·7	1·3	0·3	2·85	
2785/50 ..	7·1	0·7	0·8	10·14	
3887/49 ..	8·4	1·9	1·3	4·42	
1959/49 ..	27·3	3·9	1·0	7·00	
9201/47 ..	11·0	7·1	0·6	1·55	7·38

been taken. The ratio between the amount in the liver and that in the kidneys has even less significance in respect of the amounts that may have been ingested. As Webster[7] rightly points out, in cases where death is relatively rapid, the rule is that the liver, kidneys and spleen contain a greater proportion of arsenic than an equal weight of muscle, brain or other tissue but, if death is delayed for some days, there is a tendency towards a more equal distribution of arsenic in the different organs. As an extreme example, this point is illustrated when considering the 'normal' arsenic content of the various tissues, as shown in Table I, where the amount varies between 0.2 and 0.4 p.p.m.

In this connexion it must be pointed out that a more satisfactory basis of comparison is in terms of concentration of arsenic in the organs rather than in terms of absolute amounts. In this way differences between the weights of the various organs in each individual case and between the individuals in different cases are eliminated. In the remainder of this paper, therefore, the data will be discussed on the basis of parts per million (p.p.m.) or mg. per kg., unless otherwise specifically stated.

The tendency to attain a more equal concentration of arsenic in the organs after some time has elapsed is shown in Table III, where the cases have been classified into two groups, as indicated.

As might be expected, these results show that the concentration of arsenic in the organs tends to fall with the lapse of time. During this period of decrease of concentration of arsenic in the liver, the kidneys continue to act as the main source of elimination and the concentrations in these two

Table III: Distribution of Arsenic in Organs

Case	*Liver (L)*	*Kidneys (K)*	*Stomach*	*Ratio L : K*
A: Death up to 8 Hours				
2801/52 ..	59·5	23·6	840·0	2·52
2569/52 ..	158·1	38·0	56·7	4·11
4994/51 ..	517·8	171·6	8271·5	3·02
2016/51 ..	115·0	47·3	167·3	2·43
4905/50 ..	28·3	12·4	38·5	2·00
697/50 ..	21·1	9·2	18·6	2·30
6923/49 ..	91·0	14·4	13·3	6·32
2232/49 ..	28·2	11·3	21·6	2·50
259/49 ..	49·6	144·6	81·3	0·34
9227/49 ..	53·3	23·6	35·4	2·26
3360/48 ..	20·1	10·8	296·7	1·86
5216/48 ..	86·0	204·5	39·1	0·84
6822/48 ..	465·3	471·7	1400·0	0·99
Average ..	130·3	91·0		2·42
B: Death After 2 Days or More				
8500/52 ..	5·5	23·6	4·1	0·23
6387/52 ..	7·7	2·7	—	2·98
5190/51 ..	5·3	4·0	2·0	1·33
1536/51 ..	8·0	13·7	5·2	0·58
4711/50 ..	21·4	15·0	4·0	1·43
2785/50 ..	3·8	1·9	3·0	2·00
8415/49 ..	41·8	371·7	10·0	0·11
3887/49 ..	8·1	8·3	3·3	0·99
1959/49 ..	21·3	18·0	3·5	1·18
3997/48 ..	11·3	30·9	1·8	0·37
9201/47 ..	9·3	5·5	3·4	1·70
Average ..	11·0	44·1		1·17

organs tend to become more nearly equal than in the early stages of poisoning. The average values for the value of the ratio L : K are 2.43 and 1.17. The difference is 1.25 and, as a measure of the significance of this difference, the value 't' as described by Fisher[2] was found to be 2.36. For a 20 : 1 probability that this is not due to chance the value should be 2.07. The difference is therefore significant and the trend towards a levelling of the concentration in the organs is thus real and significant. It is clear from the Table that the concentration of arsenic in the liver decreases, but it can be shown that there is no significance in the difference between the concentrations of arsenic in the kidneys in the above two groups. The value of 't' for the difference is only 0.95. The kidneys thus continue to function as the main source of elimination even after the lapse of some time.

However, the ratio L : K is not correlated with the amounts or concentration of arsenic in the liver. The correlation coefficients 'r' between the amounts of arsenic in the liver and the value of the ratio L : K were found to be +0.18 and −0.30 for the two groups respectively. For significance, the values of 'r' should be 0.55 and 0.60 respectively. It

would thus be useless to attempt to judge the amount of arsenic taken from the value of this ratio. It is not even related to the amount actually present.

The time factor is obviously correlated with the rate of absorption but this, again, is subject to so many other variables that it would be impossible to arrive at any satisfactory figure for the amount of arsenic taken from the amount present in the liver or in the kidneys at the time of death. Even an analysis of the whole body would indicate only the total amount of arsenic present in the body at the time of death, but would not indicate in any way the amount of arsenic originally ingested unless it were possible to determine the amount eliminated from the system through the usual channels before death has occurred. The effect of the time factor upon the value of the ratio L : K is illustrated in somewhat more detail in Table IV where the ratios have been grouped according to times before death. Cases involving children have been excluded.

Table IV: Ratio L : K According to Time

	4 Hours	8 Hours	12 Hours	24 Hours	2½ Days	5 Days	> 5 Days
	2·52	2·43	2·71	3·67	2·45	0·23	2·98
	3·02	2·30	1·61	0·90	0·54	1·33	2·98
	2·00	6·32		4·41	0·32	0·58	1·18
	9·71	0·34		0·62		0·99	0·37
	5·05	2·26		1·60			1·70
	0·30	1·86		1·80			
	2·50	0·84		2·45			
	2·11						
	0·99						
Average	3·13	2·35	2·16	2·21	1·10	0·78	1·65
Cases	9	7	2	7	3	4	5

It will be seen that there is a general tendency for the concentrations of arsenic in the liver and in the kidneys to become equal after some time has elapsed but it is also clear that there are very wide variations in each group. It is interesting to note that out of the 37 cases recorded, death has occurred within 12 hours in 18 cases and that 12 victims have survived for 24 hours or longer. These circumstances may have an important bearing upon the chances of saving life in cases of arsenical poisoning provided that the victim has survived the initial critical period, that the correct diagnosis has been made and that the appropriate counter-measures have been taken. It is also clear, however, that the individual variations are somewhat large and the circumstances of the case must play an exceedingly important part in any decision which may have to be taken. The absolute amount of arsenic in the liver will, of course, depend greatly upon the weight of that organ and the amount ingested, but the concentration will, in effect, be the vital factor.

It is difficult to correlate the amount of arsenic in the liver with time.

In the very early stages of poisoning the rate of storage of arsenic in the liver will depend upon the amount of arsenic absorbed from the gastro-intestinal tract and the ratio L : K will tend to increase. Accumulation in the liver will continue as long as any arsenic remains in the gastro-intestinal tract. At the same time, the kidneys will begin to excrete arsenic and the ratio will depend upon the result of these two opposing factors. This condition is illustrated to some extent in Table IV where the values for the ratio L : K show extremely wide variations at the different times Thus any attempt to correlate this ratio with time must be doomed to failure.

Effect of Age upon the Distribution of Arsenic

It is perhaps interesting to compare the analytical results obtained for children with those for adults in cases of death from arsenical poisoning. In this case, it is essential to make the comparison on the basis of concentration, i.e. in terms of parts per million. The data available for the period 1948-1952 are given in Table V.

Table V: Death of Children from Arsenical Poisoning

Case	*Age in Years*	*Time of Death*	*Liver (L)*	*Kidneys (K)*	*Stomach (S)*	*Ratio L : K*
7177/52 ..	2	—	4·3	0·8	3·2	5·38
1536/51 ..	5	5 days	8·0	13·7	5·2	0·58
4520/50 ..	7	5 hours	23·4	13·7	13·0	1·76
4617/50 ..	(Child)	1½ hours	17·3	12·5	4·4	1·38
697/50 ..	6	6 hours	21·1	9·2	18·6	2·29
8189/49 ..	5	2½ days	10·4	7·2	10·0	1·44
8415/49 ..	9	2 days	41·8	371·7	10·0	0·11
2329/49 ..	9	4 hours	17·6	15·8	29·0	1·11
1452/49 ..	(14 days)	—	24·0	4·3	6·5	5·69
9327/47 ..	2	8 hours	53·3	21·6	35·4	1·85
4490/48 ..	2	24 hours	3·0	3·5	1·2	0·86
610/48 ..	3	7½ hours	30·9	16·7	4·0	1·85
3193/48 ..	5	—	84·5	26·0	40·0	3·25
Average ..			26·1	39·8		2·11

On comparing these results with all the data given in Table III it would appear that the concentrations of arsenic in the liver and kidneys (76.9 p.p.m. and 70.0 p.p.m. respectively) are higher than for children (26.1 p.p.m. and 39.8 p.p.m. respectively for the liver and kidneys) and this may point to a more sensitive physiological mechanism in the case of children. However, it is interesting to note that there is no significant difference in the values of the ratio L : K. The difference in the average values is 0.26 with a value of 0.5 for '*t*', indicating that no significant difference exists in the distribution.

Effect of Similar Circumstances in Administration

It is a matter of some interest to ascertain how far similar conditions surrounding death from arsenical poisoning may influence the distribution of arsenic in the system. In Table VI the results have been tabulated for cases where two or more deaths have occurred under more or less identical conditions. The data are expressed, as before, in terms of parts per million to eliminate variations due to the different weights of the organs.

Table VI: Death under the Same Circumstances

Case	*Age in Years*	*Time of Death*	*Liver (L)*	*Kidneys (K)*	*Stomach (S)*	*Ratio L : K*
8063/52 ..	2	4 hours	37·3	60·0	603·0	0·62
,, ..	2½	6 hours	17·8	9·2	10·0	1·94
1903/52 ..	7	6 hours	20·8	3·5	24·6	5·94
,, ..	3	6 hours	31·2	6·1	52·0	5·12
,, ..	4½	6 hours	11·9	37·4	4·9	0·32
,, ..	12	24 hours	11·4	34·5	2·1	0·33
4711/50 ..	2½	2 days	21·4	15·0	4·0	1·43
,, ..	6	1 day	10·4	32·5	74·3	0·14
4434/49 ..	Adult	1 hour	14·9	49·5	373·0	0·30
,, ..	,,	1 hour	152·0	865·1	—	0·18
1207/48 ..	Adult	24 hours	8·1	13·0	22·5	0·62
,, ..	,,	24 hours	78·4	49·4	122·4	1·59
4281/48 ..	Adult	—	7·4	6·5	1·1	1·14
,, ..	,,	—	15·3	11·8	2·4	1·30
4367/48 ..	Adult	4 hours	23·6	11·2	7·6	2·10
,, ..	,,	24 hours	55·5	22·6	64·7	2·45
5425/48 ..	5	17 hours	17·9	30·8	2·9	0·51
,, ..	10	18 hours	29·7	15·5	7·9	1·91

It can be seen that no hard and fast rule can be laid down concerning the distribution of arsenic in the system. The data can only be regarded as evidence of the highly variable character of biological systems. The concentrations do not appear to be related either to the age or to the time of death and, even accepting the fact that the amounts ingested are not necessarily identical in the cases, the ratio L : K indicates clearly how widely the distribution may vary in any particular case. Cases No. 8063/52, 1903/52, and 5425/48 provide good examples of this variation.

The difficulty of predicting the course of absorption is clearly evident in Case No. 1903/52 where 4 children died from drinking water containing 0.02% of arsenious oxide. The amounts of arsenic recovered from the liver, the kidneys and the stomach were 11.3 mg., 18.6 mg., 11.1 mg. and 6.3 mg. respectively. It will be noted, however, that the values of the

ratio L:K bears no relation to this sequence. Age apparently is not important as can be seen on comparing the data for the 3-year-old with those for the 4½-year-old.

Case No. 1207/48 is of interest on account of the fact that the arsenical preparation, a solution of sodium arsenite, was self-administered in the form of an enema. The results indicate that absorption from the intestinal tract has been different in each case. In the first case 118.2 mg. of arsenic were recovered from the liver, kidneys, stomach and intestines while, in the second case, 105.2 mg. were recovered from the same organs. In the first case 101.4 mg. were recovered from the intestines alone while in the second case only 26.6 mg. were recovered from this organ. It seems clear, therefore, that absorption from the intestines has been more rapid in the latter case than in the former case. This has led to an entirely different distribution of arsenic in the system and emphasizes the difficulty of drawing any definite conclusions.

The Results of Arsenical Injection

The use of organic arsenicals as injections in the treatment of venereal diseases introduces a complication into the problem of arsenical poisoning. As these compounds are usually less toxic (weight for weight) than inorganic arsenical compounds, it might be expected that reasonable amounts of arsenic could accumulate in such organs as the liver and kidneys. The results for such cases as have been examined during the period 1948-1952 have been given in Table VII and provide a very interesting comparison with the data which have been given in previous tables.

Table VII: A: Mg. of Arsenic per Organ

Case	*Age*	*Liver (L)*	*Kidneys (K)*	*Stomach (S)*	*Intestines*	*Total*
1215/48	Adult	11·7	—	2·6	—	14·3
1912/48	Adult	71·5	26·0	13·0	37·0	149·5
2009/48	Child	9·7	—	—	—	9·7
6377/49	Adult	1·5	0·3	0·07	—	1·87
272/52	Child	2·2	0·19	0·13	1·3	3·82
593/52	Child	1·2	0·19	—	—	1·39
634/52	Child	1·5	0·19	—	—	1·69

B: Parts per Million of Arsenic

Case	*Age*	*Liver (L)*	*Kidneys (K)*	*Stomach (S)*	*Ratio L : K*
1215/48	Adult	10·2	—	20·0	—
1912/48	Adult	88·3	86·7	40·3	1·02
2009/48	Child	51·0	—	—	—
6377/49	Adult	1·2	1·8	0·3	0·67
272/52	Child	8·6	3·2	2·9	2·70
593/52	Child	5·5	4·8	—	1·15
634/52	Child	8·0	3·2	—	2·50
Average					1·61

The total amounts recovered are not comparable since, in several cases, all the usual organs were not submitted. However, in Cases Nos. 1215/48, 1912/48 and 2009/48 it will be noted that as much as 11.7 mg., 71.5 mg. and 9.7 mg. were recovered from the liver alone. It would also appear from the value for the ratio L : K that the arsenic has a tendency to be more evenly distributed in the system. However, these anti-venereal preparations are prescribed only by a medical man and are administered under supervision, so that a former history is always available. In such cases, therefore, special care must be taken in attaching significance to any but the larger amounts of arsenic. In Case No. 1912/48 it would appear that somewhat massive doses must have been administered. There was no evidence of any other source of arsenic ingestion. In cases where anti-venereal arsenicals have been used, it is sometimes possible to determine whether organic arsenic as such is present in the urine. This, however, is a somewhat rare occurrence even in special circumstances.

Analytical Data in Relation to Murder or Suicide

Statements have sometimes been made that it is possible to deduce from the analytical data, especially from the ratio of the amount in the liver to the amount in the stomach, whether the poison has been self-administered or not. Another opinion is based on the assumption that self-administered doses are always greater than those administered secretly in murder, and that, therefore, higher amounts are always recovered in cases of suicide or self-administration. Although the latter opinion may appear to be logical, there is, in our experience, no ground for either statement. In South Africa the assumption that self-administered doses are always greater than those administered with illegal intent falls away to a large extent since the Native, who is largely responsible for cases of homicide by poison, has little conception of quantity, nor does he possess adequate means for measuring any dose which he may desire to administer. Another important factor lies in the nature of the physiological action of arsenic. It has powerful irritant and emetic properties and the larger the amount ingested the more violent is likely to be the reaction. The larger doses are therefore more likely to be eliminated rapidly by vomiting and purging than smaller doses. In Table VIII the results have been given for the period 1948-1952 for cases of suicide as well as for an equal number of cases of homicide, chosen at random. The data are given in terms of parts per million except in the case of the total amount of arsenic recovered from the liver, the kidneys and stomach which are recorded in mg. Cases of exhumation have been excluded from the table.

A cursory glance at the results in Table VIII will be sufficient to dispel the ideas concerning the distinctions to be made between suicide and murder. There is only one case where any such decision might be made

Table VIII: A: Suicides

Case	*Total*	*Liver (L)*	*Kidneys (K)*	*Stomach (S)*	*Ratio L : K*	*Ratio L : S*
3360/48	57·8	20·1	10·8	298·7	1·87	0·07
8260/49	8541·0	602·9	704·8	25560·0	0·86	0·02
8290/49	14·5	9·6	5·2	3·3	1·85	2·91
4401/49	60·0	31·8	7·0	13·2	4·84	2·41
2562/49	65·6	21·0	13·0	20·5	1·61	1·02
2606/49	18·9	11·1	5·0	2·0	2·22	5·55
287/49	30·5	24·3	9·5	2·4	2·56	10·12
367/49	30·2	22·1	7·7	16·0	2·87	1·38
7015/50	14·6	8·4	9·3	1·6	0·90	5·25
7140/50	19·5	14·8	27·3	5·8	0·54	2·55
5758/51	142·9	22·8	15·6	261·5	1·46	0·11
5500/51	726·7	130·0	47·3	1520·4	2·73	0·09
8690/52	36·3	23·8	11·6	7·1	2·05	3·55
2801/52	282·7	59·5	23·6	840·0	2·52	0·07
9463/52	51·3	42·5	17·3	11·5	2·46	3·70
6/52	27·2	15·1	12·6	5·5	1·20	2·75
Average	632·5				2·02	2·60
		B: Murder				
3415/48	57·8	35·3	19·6	11·3	1·80	3·21
5216/48	143·5	86·0	409·0	39·1	0·21	2·20
6822/48	813·5	463·1	471·7	1400·0	0·98	0·32
7041/49	7·0	4·8	2·6	1·9	1·85	2·53
6923/49	117·0	91·0	14·4	13·3	6·32	6·84
3591/49	304·7	75·3	34·0	156·2	2·22	0·48
4697/49	419·2	122·0	39·6	276·8	3·08	0·44
259/49	131·7	49·6	144·6	81·3	0·34	0·61
4905/50	52·0	28·3	12·4	38·5	2·00	0·74
697/50	11·0	21·1	9·2	18·6	2·30	1·13
8520/49	20·2	17·4	3·2	1·9	5·44	9·16
4994/51	2623·3	517·8	171·6	8271·5	3·02	0·06
2016/51	178·6	115·0	47·3	167·3	2·43	0·69
8829/52	40·2	30·8	5·5	84·3	5·60	0·37
2569/52	217·4	156·1	38·0	56·7	4·16	2·79
350/52	48·7	28·6	7·8	52·0	3·54	0·55
Average	324·1				2·83	2·02

namely, Case No. 8260/49. This is a quite abnormal case and yet is very closely matched by Case No. 4994/51. Even considering the total amounts of arsenic recovered from the liver, the kidneys and the stomach there is no significance in the difference between the average amounts recovered in the case of suicides and murders. The values are 632.5 mg. and 324.1 mg. respectively but the value of 't' for the difference is only 1.18, and this should be 2.04 for a 20 : 1 chance of significance.

The average values of the ratio L : K are 2.02 and 2.83 for suicides and murders respectively. The value of 't' for the difference is 1.39 as compared with 2.04 for a 20 : 1 chance of significance. In the case of the ratio L : S the difference is 0.58 with a value of 't' of 0.62 which also has no significance when compared with the value of 2.04 for a 20 : 1 chance of significance. It is thus perfectly clear that any assumptions that

the analytical results can distinguish between suicide and murder are based upon reasons which have no foundation in practice. General conclusions simply cannot be made unless all the surrounding circumstances are known. Such circumstances cannot be elucidated solely by an analysis.

Arsenical Poisoning in Relation to the State of the Corpse after Burial

A statement which is frequently made and, in view of its authoritative source, is tenaciously held, is that a well-preserved state of the corpse, particularly after burial, is a clear indication of death from arsenical poisoning. When, however, the relatively large amounts of arsenic used in embalming are considered, it becomes difficult to see how the amounts of arsenic usually found in viscera in cases of arsenical poisoning can have any appreciable effect in preventing decomposition of the body after death. In order, however, to examine this problem in more detail cases of exhumation during the period 1948—1952 have been given in Table IX where the period of burial has been up to one year. When exhumation has been carried out after a year or more, it can be expected that the natural processes of decomposition and dehydration will be sufficient to account for any changes that may, or may not, have occurred. The disappearance of the soft tissues can be expected as a natural consequence of the passage of time. In Table IX the observations of the District Surgeons have been quoted together with the analytical data. In addition, the symptoms of vomiting and/or purging, usually associated with arsenical poisoning, have been included when such information has been supplied. The data are reported in terms of mg. per organ since changes in the weights of the organs, due to losses of moisture, do not permit the results to be given correctly in terms of p.p.m. for the original organs.

Table IX: Exhumations (Arsenic Present)

Case	*Time*	*Symptoms*	*Liver*	*Kidneys*	*Stomach*	*Total*	*Observations*
2761/52	6—7 days	V	49·4	1·9	20·1	71·4	Putrefaction well advanced.
5543/51	5 days	V	7·1	1·3	9·7	18·1	Preserved but changes evident.
6410/50	6—7 days	V & P	16·2	1·5	0·3	18·0	Putrefaction starting.
3151/50 (X)	6 days	V & P	32·5	2·6	5·8	39·9	Very advanced putrefaction and decomposition.
75/50	4 days	V & P	27·9	0·3	0·7	28·9	Advanced putrefaction.
5996/49	12 days	V	—	2·3	2·8	—	Advanced decomposition.
4563/49 (X)	6 months	V	6·5	—	1·3	—	Advanced decomposition.
4095/49	8 days	—	3·2	—	9·1	—	Unusually well preserved.
2963/48	2 months	—	233·6	16·2	317·4	567·2	External decomposition well advanced otherwise less than anticipated.
3546/48	5 months	V & P	201·5	11·0	52·6	265·1	Good state of preservation.
3625/48	6 months	V & P	37·7	—	2·1	—	Fair preservation, major portion mummified.
5928 48 (X)	3 days	V & P	1·6	0·2	0·7	2·5	Well preserved.
7046/48	3 weeks	V	13·0	0·9	0·8	14·7	Advanced putrefaction.
3193/48 (X)	2 weeks	P	84·5	26·0	40·0	144·5	Advanced putrefaction.

X = Child; V = Vomiting; P = Purging.

Of the 14 cases reported in Table IX, six may be considered as 'preserved'. From Cases No. 2963/48 and No. 3546/48 567.2 mg. and 265.1 mg. of arsenic respectively were recovered from the liver, kidneys and stomach. These amounts are relatively large in comparison with the amounts usually found in cases of arsenical poisoning. Even so in Case No. 2963/48 'external decomposition' was 'well advanced'. In Case No. 5543/51 only 18.1 mg. of arsenic were recovered from the liver, kidneys and stomach, while in Case No. 4095/49 where the body was 'unusually well preserved' only 12.3 mg. of arsenic were recovered from the liver and stomach. It would appear, therefore, that the state of preservation of the body is not directly associated with the presence of arsenic in the system. In Case No. 5938/48, which was that of a child, only 2.5 mg. of arsenic were recovered and yet the body was well preserved. In Case No. 3625/48 there was 'fair preservation' of the body with the 'major portion being mummified' and 39.8 mg. of arsenic were recovered from the liver and stomach. These results would seem to point to dehydration as an important factor in preserving the body after burial. In all the cases, except Cases No. 4095/49 and No. 2963/48, there was evidence of vomiting and/or purging before death.

The remaining eight cases recorded in Table IX are described in terms of 'decomposition' and 'putrefaction', generally 'advanced'. In this connexion it is interesting to compare Case No. 3193/48 with, say, Case No. 4095/49. In the former case 11.05 mg. were recovered from the liver and stomach while, in the latter case, only 12.3 mg. were recovered from the same organs and yet the latter was described as 'unusually well preserved'.

In order to obtain some further information concerning the problem of the preservation of the body after burial, some cases of exhumation are given in Table X where arsenic could not be detected in the viscera. The remaining cases in this category have all been described in terms of 'advanced putrefaction'.

Table X: Exhumation (Arsenic Absent)

Case	*Time*	*Symptoms*	*Observations*
1380/52 ..	2 days	—	State of preservation of body good but putrefactive changes present in viscera.
1763/52 ..	3½ years	V	State of desiccation (organs indentifiable).
7874/51 ..	5 days	—	Putrefaction starting.
8395/51 ..	3 months	P	Signs of decomposition.
7357/51 ..	2 months	—	Body recognizable and externally mummified; some decomposition in organs but could be examined.
5292/50 ..	5 weeks	—	Well preserved.
7150/49 ..	2 weeks	—	(Organs submitted separately.)
7070/48 ..	5 days	—	Slightly decomposed.
4687/48 ..	7 days	V	Moderate putrefaction; liver normal.
3988/48 ..	6 months	—	Partly decomposed.
5272/48 ..	3½ weeks	V	Remarkably well preserved.
6582/48 ..	2 months	—	Remarkable state of preservation.

A comparison of the 'Observations' in Table IX and X will indicate remarkably little difference in the descriptions of the state of the bodies after burial. In Case No. 7150/49 no special observations were made concerning the state of preservation of the body but, since the various organs were submitted separately, it is logical to assume that they were sufficiently well preserved to permit of identification.

Cases No. 5292/50, No. 5272/48 and No. 6582/48 are good examples of preservation of the body even in the absence of arsenic. In Case No. 6582/48, the body was buried in dry sandy ground and, in addition, arsenic was absent from the hair and nails, so that there can be no question even of chronic arsenical poisoning.

It is perfectly clear, therefore, from the above data that no reliance can be placed upon the state of preservation of the body as an indication of arsenical poisoning. The causes of preservation must thus be sought in factors other than the mere presence of arsenic in the system. It is suggested that dehydration may be one such factor.

Diagnosis of Arsenical Poisoning

The symptoms and post-mortem appearances in cases of acute arsenical poisoning are such that they may well be duplicated by most other irritant poisons, and these circumstances introduce so many complications into the problem of diagnosis that great caution must be used in arriving at any definite decision. The interpretation of a case of suspected arsenical poisoning, according to Webster,[6] should rest on both the chemical and post-mortem findings, as many anomalous cases will be found in which somewhat typical clinical signs will be present without the usual autopsy findings while, in other cases, the reverse will occur. In such cases chemical examination of the tissues will be required to solve the question involved. Therefore, definite conclusions that death was due to acute arsenical poisoning must ultimately depend upon the results of a chemical examination of the organs. Webster[6] maintains that, as many cases of acute arsenical poisoning show a delay in the appearance of symptoms, this is evidence that the toxic action of arsenic is actually a result of action after absorption and not a consequence of direct gastro-intestinal irritation. In the case of chronic arsenical poisoning there are other clinical symptoms which assist in building up a more certain picture of poisoning.

Vomiting and purging are usually regarded as probable indications of arsenical poisoning and yet, out of 115 cases, in which both vomiting and purging occurred, in only 32 cases was arsenic found to be present in the viscera. Of 240 cases in which vomiting only was reported, there were 38 cases only where arsenic was found to be present. During the period 1948—1952 there were 39 cases of arsenical poisoning in which neither vomiting nor purging was reported to have occurred.

A very similar picture can be drawn from the post-mortem findings as reported to this laboratory. Haemorrhagic signs and congestion in various organs are of such common occurrence in cases of violent death from poisoning, particularly in the cases of irritant poisons, that it seems almost impossible to arrive at any definite conclusions concerning the exact nature of the poison responsible for these signs. Unless there is some direct evidence that some arsenical preparation has been administered to the deceased, the District Surgeon is on somewhat unsafe ground when he makes a direct request for an examination for arsenic on the basis only of symptoms of vomiting or purging or on the basis of his post-mortem findings. This conclusion is supported by the data provided in Table XI of examples where the 'requests' are compared with the chemical 'findings'.

Table XI: Post-Mortem Appearances

Case	*Request*	*Results*
2140/51	Arsenic or Alkaloid	Negative
3987/51	Arsenic or Cantharidin	Negative
1729/50	Arsenic or strychnine	Negative
2309/51	Arsenic	Barbiturate
9201/47	Arsenic or strychnine	Arsenic
6470/48	Arsenic or similar poison	Barbiturate

It is clear from Table XI that there must be some cause for confusion in the post-mortem appearances. Of 68 cases where arsenic was directly suggested as the poison only 27 proved to be positive for arsenic. In one of the 68 cases a chromium compound was the cause of death; in another fluorine was found to be present; in two cases cantharidin was the cause of death while one case was a case of so-called 'food' poisoning. In these cases, the symptoms and, it must be presumed, the post-mortem appearances were similar and such as to suggest arsenical poisoning in a general way.

These observations and remarks are put forward to indicate the difficulties associated with the detection of acute arsenical poisoning. It is therefore essential that the fullest information possible concerning the whole history of a case and the detailed circumstances be submitted to assist the analyst in his examination of the organs. This requirement is applicable not only in cases of suspected arsenical poisoning but to all poisons and cannot be over-stressed in view of the multiplicity of poisonous chemicals which have become available during the last decade. It is a *sine qua non* in all cases of suspected poisoning.

Hair and Nails

The fact that arsenic tends to accumulate in the hair and nails offers a very useful method of detecting arsenical poisoning either in cases of

chronic poisoning or after some time has elapsed since administration. Generally it takes about 12 days before sufficient arsenic enters the lower portion of the hair above the scalp to enable it to be determined. For this reason it must be pointed out that it is useless to submit samples of hair in cases of acute poisoning since there will not have been sufficient time for the arsenic to be deposited in the hair appearing above the scalp. Little hair is needed for the purely qualitative detection of arsenic but, as arsenic is normally present in the hair to the extent of about 5 p.p.m., detection alone is of little value and a quantitative determination is essential. For this purpose a sample of hair containing, at the very least, 0.002 mg. of arsenic is required. It is always advisable to take *at least* 0.5 gm. (about 10 grains) of hair for a single determination and sufficient hair should be submitted for this to be done.

Since the rate of growth of hair is about half an inch per month, it is possible (by subdividing the hair into half-inch sections) to arrive at an approximate estimate of the time when administration first occurred in cases where death has been delayed for some considerable time. Given sufficient hair, further subdivision could be made but, since the rate of growth varies with individuals, no great advantage would be gained by such further subdivision. It must be borne in mind that after 12 days the arsenic will only be present in that portion of the hair above the scalp which represents the growth since the time of ingestion of the arsenic. This portion therefore is the most important portion of the hair for the purpose. In taking samples of hair for examination, therefore, the possibility of subdivision should be borne in mind; the sample must be so tied that the root portions are kept together and sufficient of the sample must be submitted to enable subdivision to be made. An endeavour should always be made to collect a bunch of hair about the thickness of a finger. These remarks are obviously not generally applicable to hair from a Native but, nevertheless, sufficient hair in such a case must be submitted to provide the required minimum amount of about 0.5 gm.

An investigation of the nails in cases of chronic or subacute arsenical poisoning presents somewhat greater difficulties than does the hair, owing to the relatively small amounts of nail which can be obtained in such cases. The arsenic deposits in the early stages in the nail tissue just below the skin and a considerable period elapses before such arsenic-impregnated nail tissue reaches the tip of the nail. If the problem of prior administration arises in cases of death from arsenical poisoning then, of course, whole nails can be removed and should be submitted.

In connexion with the actual determination of arsenic in exhibits such as hair and nails it is usual and essential to clean the samples thoroughly with dilute reagents to eliminate as far as possible adventitious contamination, before any attempt is made to determine the arsenic content.

An example of an investigation involving the subdivision of hair has

been recorded in a previous paper.[1] The results obtained in a well-known case in recent years are given in Table XII as an example of the type of results which may be obtained in cases of prior administration. The results are given in terms of parts per million.

Table XII: Arsenic in Hair and Nails
(Rex *v.* Lee, 1948, Cape Provincial Division of the Supreme Court of South Africa)

Hair	*Arsenic*	*Nails* *Thumb*	*Right Toe*	*Left Toe*
1st ⅛ inch	250	Base 748	634	688
2nd „	92	Middle 142	100	133
3rd „	95	Top 143	133	85
4th „	86			
5th „	69			
6th „	66			
7th „	65			
Top 1 inch	27			

The results are relatively high and indicate clearly that there must have been prior administration some considerable time before death. In this case 26.6 mg. and 35.7 mg. were found in the liver and stomach respectively, indicating that a dose of arsenic must have been administered not long before death. A fairly high concentration of arsenic must have existed in the system and this, together with the fact that the hair was pulled from the scalp at the time of examination, probably accounts for the exceptionally high figure for the arsenic content of the first ½-inch of the hair.

In another case, a bunch of hair was cut from the head of a woman who had been administered a single dose of arsenic about 5 months before; 35.0 p.p.m. and 34.6 p.p.m. of arsenic were found in the first and second inches of hair away from the scalp respectively. These results indicate administration of arsenic for some considerable time and the police were informed that 'provided the hair was cut close to the scalp adminstration of arsenic must have occurred *about* six months before the sample was taken'. The subsequent Court proceedings confirmed this suggestion.

v. Itallie[8] claims that not only is it possible to determine the time of administration, but that the amount in the hair shows a rise and fall in proportion to the amount of arsenic absorbed. No direct experience of cases of this nature has been encountered in this laboratory and the results recorded in Table XII, for example, do not indicate any such breaks in the administration. Any storage of arsenic in the organs would serve as a source for deposition in the hair and nails and this would tend to 'flatten' out any tendency to intermittent deposition in the hair and nails. Such results would, however, if confirmed, be useful to determine whether the patient had suffered from more than one dose of arsenic with an intervening long period of time.

Contamination from Soil in Exhumation

The problem always arises of exhumation involving suspected arsenical poisoning and it is therefore necessary to take samples of soil from round the coffin in such cases. If such samples are free from arsenic, the possibility of arsenic having found its way from the graveyard soil into the body does not arise. Due to the leaching of the body fluids, it is, of course, possible that the soil underneath the coffin might show traces of arsenic and such a result can obviously be expected. A case such as No. 5976/49 affords an example of this phenomenon. Traces of arsenic were detected in the soil below the grave but samples of soil a few feet away from the grave were found to be free from arsenic. In all the other cases of exhumation during the period 1948—1952 where samples of soil were submitted for examination, no arsenic could be detected in the soil. Case No. 6107/49 affords an example of the leaching of the body fluids into the surrounding areas. Exhumation was carried out after 3 years burial and the pelvic stomach and abdominal cavities were found to contain 8.9 mg. of arsenic. The shroud was found to contain 150 p.p.m. of arsenic while the lining of the coffin together with the shavings contained 26 p.p.m. of arsenic. The wood of the coffin and the surrounding soil were free from arsenic and there is no doubt that the arsenic, as found, must have come from the body.

In practice the leaching from the soil into the body is mainly of academic interest since heavy and medium soils have such a high absorptive capacity for arsenic that it is practically impossible for arsenic to leach through to the remains in the coffin. Even so, it is necessary to bear such possibilities in mind and be prepared for the inevitable questions by taking the necessary samples of soil from above and below the body as a precaution. In this connexion, due regard must, of course, be paid to such factors as rainfall, condition of the coffin, contamination of the body by the soil, etc. in considering the possibilities of contamination of the body in cases of exhumation.

Arsenic in Relation to Other Poisons in South Africa

In order to complete this survey of arsenical poisoning in South Africa an analysis was made in broad groups of the incidence of poisoning by various substances during the period 1948—1952 and the results are given in Table XIII.

As there are very many poisons which are used only occasionally these have been classed under 'Miscellaneous'. It must also be remembered that there are many cases of plant poisoning where it is not possible to identify the active principle with any certainty and such cases have been included in the 'Negative' group.

It is interesting to compare the data in Table XIII with the similar data

Table XIII: Incidence of Poisoning in South Africa (1948—1952)

Substance	1948	1949	1950	1951	1952	*Total*
Arsenic	29	36	22	8	20	115
Cantharidin ..	12	1	5	3	2	23
Strychnine	6	5	7	6	4	28
Metallic	2	7	3	6	16	34
Barbiturate	13	22	23	29	25	112
Miscellaneous ..	10	23	20	23	29	105
Negative	128	129	147	134	115	653
Total	200	223	227	209	211	1070

given in a previous paper.[1] It will be seen that arsenic still occupies a prominent place in the list of poisons used in South Africa. There has, however, been a great increase in the number of cases of barbiturate poisonings. The number of cases of poisoning by cantharidin has decreased but there has been an increase in 'metallic' poisonings, due largely to the greater use of potassium bichromate by Natives. This, once again, is a further example of the attraction which irritants have for the Native mind.

The authors would like to thank those members of the Toxicological Section of the Government Laboratories, Johannesburg, who have supplied the detailed data required for the compilation of this paper.

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Lower Nephron Nephrosis†

Its Incidence in Forensic Autopsy Material

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In 1946 Lucké [11] introduced the term *lower nephron nephrosis* (l.n.n.) for the clinical picture and associated pathological changes seen in cases of acute oligoanuria caused by a variety of injuries and diseases in patients without previous renal disease. The condition had been described earlier under different names, e.g. after the first World War, but failed to arouse greater clinical interest. It was the 1939-45 war which suddenly made l.n.n. a sharp reality. Lucké, whose series comprises more than 500 autopsies, states that 15% of all traumatic deaths during the war were due to l.n.n.

The interest in l.n.n. was soon traced in Danish publications.[1, 3, 4, 6, 9] Earlier descriptions are also to be found in Danish literature, particularly in the numerous reports of sulfa complications,[5, 13, 14] but even as early as 1935 Husfeldt and Bjering[7] described two cases which were typical both as far as the clinical picture and the autopsy findings go.

Lengthy discussion of the extensive literature on l.n.n. will be avoided. Instead reference is made to Baden and Harrestrup Andersen [1, 6] and Brun,[4a, 4b] who have given detailed surveys. Among foreign authors special mention is made of Oliver *et alii*.[12]

As far as etiology, pathogenesis, clinical picture, and treatment are concerned only a short résumé will be given. Lucké mentions the following causative factors: severe muscle trauma, muscle ischemia, burns, transfusion with incompatible blood, heat stroke, black water fever, toxemia of pregnancy, uteroplacental damage, alkalosis, sulfa treatment and poisoning; in other words, conditions in which there are often shock and/or destruction of tissue. As a rule the state of shock is successfully combated only to have oliguria, and eventually anuria, set in. Before anuria, hematuria, proteinuria and a low specific gravity may be found. Edema is seen and

† English writers have recently suggested the more accurate term 'Acute Tubular Necrosis' for this condition.—*Editor.*

* Chief: Professor Knud Sand, M.D.

not infrequently hypertension. The mortality is high if the symptoms are fully developed and death usually occurs in the course of 7-8 days. If the diuresis returns, it is often initiated by polyuria, which may lead to fatal disturbances in the fluid balance.

Pathologically the picture in typical cases is characterized by enlargement of the kidneys, the fibrous capsules being noticeably easily stripped. The surface is smooth, pale and of flabby consistency. The cortex is pale, wide, moist, swollen and contrasts sharply with the dark red medulla. The histological picture is distinguished by degeneration and sometimes necrosis of the tubuli, especially in the distal parts of the nephrons, while the glomeruli are normal. There is pronounced interstitial edema and scattered inflammatory infiltrates, especially perivascular, but also periglomerular. Casts, which are often hemoglobin stained, are found in the lower segments and in the collecting tubules.

L.n.n. appears to be increasing in frequency. This is no doubt due primarily to increased interest in and familiarity with the picture. An actual increase in the number of heavy traffic and industrial accidents, however, together with an increasing number of criminal abortions, and especially the intensive treatment which these patients and poisoning cases (particularly barbiturate cases) receive now have also to be taken into consideration. In the past many of these patients undoubtedly died as a direct result of injuries and shock, before the symptoms of l.n.n. developed. As the treatment of anuria becomes more efficient, we may hope that the condition will become rare, at least in the autopsy room.

The previously mentioned Danish publications have comprised essentially rather small groups of patients with practically uniform histories: a group of obstetrical cases, diarrhoea cases, hepatorenal syndrome, sulfa cases, bleeding ulcers, and a few others. On the other hand only a few traumatically or toxically produced cases have been reported.[4b, 7] Due to the nature of the cases, the majority undergoes forensic investigation and autopsy.

A report of the histologically verified cases of l.n.n. that have been autopsied at the University Institute of Forensic Medicine, Copenhagen, during the years 1949-53, will be given below. The cause of death in some of the cases has been l.n.n., in others l.n.n. has only been a contributing factor.

Undoubtedly one can find all degrees, from the fully developed picture to the rather mild case without clinical symptoms, which only evidences slight histological changes.

The causative factors in the 21 cases observed by us appear from the following short histories:

1. Prolonged diarrhoea in a 46-year-old woman after ingestion of a mercury preparation, supposedly to interrupt a feared but non-existing pregnancy. Death on the 7th day (?).

2. Unconsciousness in an 18-year-old woman after an attempt at suicide by means of barbiturates, for fear of a supposed but non-existing pregnancy. Patient recovered primarily, later developing l.n.n. with death on the 15th day.

3. A 37-year-old man with Addison's disease. Death on the way to hospital in Copenhagen, probably during a crisis.

4. A 32-year-old woman. Attempted abortion with bichromate of potassium. Vomiting and diarrhoea. Death on the 9th day.

5. A 62-year-old man. Various fractures after traffic accident. Shock. Transfusion reaction. Death on the 12th day, 10 days after the transfusion.

6. Abortion provoked by an unknown substance in a 32-year-old woman. Convulsions and vomiting. Death on the 9th day.

7. A 66-year-old man with extensive third degree burns. Death on the 7th day.

8. Deep unconsciousness as result of acute alcohol intoxication in connection with ingestion of allypropymal. A 56-year-old man. Death on the 7th day.

9. Severe fractures and muscle lacerations after a train accident. Shock. A 47-year-old man. Death on the 6th day.

10. Septic abortion in a 26-year-old female, produced by some unknown methemoglobin-forming drug. Treated with lucosil (a populalr sulfa-preparation) until diuresis sharply declined. Death on the 12th day.

11. Severe fractures and lacerations after an automobile accident under the influence of alcohol. Shock. A 26-year-old male. Death on the 7th day.

12. Poisoning by ammonia fumes. Vomiting, hemolytic anemia. A 32-year-old man. Death on the 22nd day.

13. A 45-year-old psychotic woman. Shock after a fall accident, may be in connection with over-sedation. Death on the 17th day.

14. A 33-year-old man. Fracture of the jaw bone and concussion. Later deep shock. Death on the 8th day, 4 days after development of shock.

15. Septic abortion produced by crochet-hook in a 25-year-old female. Vomiting. Shock. Death on the 4th day.

16. A deep unconsciousness in a 75-year-old diabetic female after CO-inhalation. Presumably no coma diabeticum. Death on the 2nd (?) day.

17. Deep unconsciousness after a traffic accident. Subdural hematoma. A 45-year-old man. Death on the 11th day.

18. Fracture of the skull after having been hit by a car. A 51-year-old man. Long-lasting unconsciousness. 15th day shock. Transfusion with good result. Thereafter oliguria. Death on the 19th day, 4 days after transfusion.

19. Bad fall from a barn loft. Shock. Retroperitoneal hematoma. Paralytic ileus. Laparotomy. A 64-year-old man. Death on the 16th day, 6 days after operation.

20. A 29-year-old man trapped in an automobile for 1 hour following an accident. Fractures with muscular lacerations. Shock. Death on the 9th day.

21. A 60-year-old man with extensive burns (30%). Local treatment with lucosil. Death on the 7th day.

Table 1 gives a survey of the clinical and autopsy data. The stated frequencies are generally to be considered minimum figures, partly because the information about the histories is sometimes wanting, partly because

Table 1

Classification	Number of cases	21
	Females	8
	Males	13
	Poisonings	9
	Casualties	11
Clinical Details	Shock (Causative factors)	14
	Dehydration (Causative factors)	5
	Vomiting (Causative factors)	7
	Development of hypertension	5
	Oliguria and/or anuria	14
	Treated with penicillin	13
	Blood transfusion given	15
	Other intravenous fluids	13
Laboratory Findings	Proteinuria	8
	Hematuria or positive benzidine reaction	6
	Elevated blood urea (61 to 581 mg. per 100 c.c.)	20
Macroscopic Autopsy Findings	Enlarged kidneys	5
	Cortex widened	4
	Cortex pale	16
	Hyperemia at the base of the pyramids	8
	Capsules easily detached	21
	Bulging of the cut surface	8
	Normal appearing kidneys	4
	Edema of the brain	15
	Edema of the lungs	18
	Peripheral edema	3
Microscopic Findings	Glomeruli normal	21 (16)*
	Interstitial edema	15
	Scattered cell infiltration	18
	Degeneration of proximal tubuli	3 (6?)
	Degeneration of distal tubuli and loops of Henle	7 (10?)
	Tubules putrefied	12
	Pigment casts in tubules	20
	Unpigmented casts in tubules	11
	Other kidney diseases (occasional hyaline glomeruli 5, pyelonephritis 1)	6

*In 5 cases an occasional hyaline glomerulus was found.

the finer histological details are lost, the medico-legal autopsies frequently not being performed till relatively late *post mortem*. The figures illustrate, however, the fact mentioned that the condition exists in all grades from the mildest to the fully pronounced.

Most of the poisoning cases are females while on the other hand the casualties are mostly males. Among the 8 women pregnancy was the underlying factor in no less than 6 cases; of these 5 were abortions and one attempted suicide. In two of these cases necropsy showed that the undesired pregnancy had not been present.

Thirteen patients had been treated with penicillin and a few with other antibiotics. It will probably be erroneous to ascribe any deleterious effects to the administration of penicillin but it demonstrates quite clearly the fact that these patients have been intensively treated so that they have not, as would frequently have been the case formerly, died from shock or infection. The vigorous treatment is furthermore demonstrated by the fact that 15 received one or more blood transfusions while 13 had other intravenous infusions.

In all 21 cases the fibrous capsules were remarkably easily detached. The cortex was noticeably pale in 16 cases, while the other characteristic microscopic changes were less frequent. Special mention must be made of the fact that in 4 cases the kidneys were found to be microscopically completely normal.

Microscopically, the most constant feature was the appearance of hemoglobin-stained pigment casts in the distal parts of the nephrons, which occurred in 20 of the cases.

When putrefaction did not make evaluation of the condition of the tubules futile, degeneration of the distal tubuli and the loops of Henle was found twice as frequently as in the proximal tubuli.

While no case showed evidence of fresh glomerular changes, 6 presented scattered hyaline glomeruli (older changes). No indication of Kimmelstiel-Wilson changes (intercapillary glomerulosclerosis) was found in the diabetic kidneys.

In the kidneys from the patient who died from mercury poisoning the typical picture of l.n.n. was present.

The characteristic scattered infiltrations of lymphocytes and macrophages were seen in 13 of the cases.

The clinical picture was typical and it was possible to explain the cause of the oligoanuria in practically all the cases.

Only one case (No. 14) will be described in detail, partly because the mechanism is not satisfactorily explained, partly because it illustrates very well the typical pronounced case of l.n.n.

A young, healthy man with no previous history of renal disease was attacked with brass knuckles which caused a triple fracture of the jaw bone. He did not

lose consciousness immediately and was able to drive to an emergency room, where the jaw bone was wired.

For the following days the temperature was elevated but the patient daily visited an out-patient clinic, where he gave the impression of having a mild concussion. He was treated with penicillin injections. On the fourth day the patient was found comatose in bed, cyanotic, with an imperceptible pulse and agonal respiration.

He was admitted to a neurosurgical department, and craniotomy was performed after aspiration of the upper respiratory passages. There was no evidence of intracranial bleeding but pronounced edema was found. Furthermore, atelectasis of the inferior lobe of one lung was found.

Under the continued treatment, which was primarily directed against the shock, anuria developed followed by peripheral edema and the development of hypertension. Despite intraperitoneal dialysis death occurred 4 days after the fatal shock. The last blood urea estimation was 325 mg. per 100 c.c.

The unusual feature in this case is the deep shock 3 days after the trauma. The explanation is probably development of delayed traumatic edema of the brain which was not diagnosed (the patient was not hospitalized) before the patient was moribund and the terminal drop in blood pressure had set in. Microscopically, no evidence of former kidney disease could be demonstrated.

The treatment of anuria will not be discussed here. The principle is to control the fluid and electrolyte equilibrium in order to keep the patient alive until the epithelium of the tubules regenerates. As far as the toxins are concerned, interest has recently been concentrated on the endogenous potassium poisoning which possibly can be treated with ion exchangers,[8] artificial kidneys, dialysis, etc. There is all the more reason for intensive treatment of these patients, as follow-ups, published by Lowe[10] and Baden and Harrestrup Andersen[2] demonstrate that the prognosis is good if the patient can be carried through the anuric phase. In almost all patients who survived, kidney function was restored completely. Several of the above-mentioned Danish articles[1, 4, 13] warn against administration of excessive fluids, so-called 'drowning'. Intensive treatment is not synonymous with abundant fluids. These warnings should no doubt be re-emphasized. In quite a few of our cases very liberal amounts of fluids had been administered.

Summary

An account is given of 21 histologically verified cases of lower nephron nephrosis seen during the years 1949-53, compiled from the files of the University Institute of Forensic Medicine, Copenhagen.

Eight cases were females, 13 males.

While the majority of the male cases was due to accident, most of the female cases were caused by various poisonings. These poisons were mainly self-administered, most frequently in order to provoke abortions or to commit suicide because of pregnancy, which in 2 of the 6 cases in this group were proven not to have been present.

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The Rh–Hr Blood Types

A Budget of Paradoxes†

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'Every branch of exact science has its paradoxers.' One has but to consult current issues of journals containing articles on blood grouping to find the sad state to which this subject has been reduced as a result of the paradoxes which currently plague it.

In 1952 a detailed explanation of the mosaic structure of red cell agglutinogens was published (Wiener and Wexler[21]) in an attempt to eliminate these paradoxes. More recently, the present author published two books[18, 19] on the Rh–Hr types, which he hoped might help to clear the air. Nevertheless, there still appears to be need for the presentation of a detailed analysis of available evidence in a manner calculated to rouse blood group workers out of their indifference to this fundamental and important problem.

The serology of the Rh–Hr types is highly complex, but one may reasonably expect a writer on this subject first to master its fundamentals. According to DeMorgan, 'All the men who are now called discoverers, in every matter ruled by thought, have been men versed in the minds of their predecessors, and learned in what had been before them.'* Blood grouping entails the use of only simple equipment—a few tubes, a pipette, a microscope, saline solution, a centrifuge and specific antisera which anyone can purchase on the open market. After a few days' practice, the beginner may imagine himself an expert in the subject, and indeed some do not hesitate to publish articles describing studies on the distribution of blood groups among individuals with various diseases or of different geographical origin. In a recent publication,[7] a series of 28 patients with Dupuytren's contracture has been reported. All the subjects are asserted to belong to type Rh_1Rh_2—a fantastic result obviously pointing to errors in Rh–Hr typing. Another author[22] claims to have established a linkage between the *Lutheran* and *Lewis* blood groups, the two systems among those known, for which the reagents available give the most unclear reactions. Some inexperienced investigators habitually report discoveries of 'new' methods, which have previously been discarded by experienced workers as unreliable, the most recent example being a revival of the method of blood typing with dried antisera on cards.[3]

On the other hand, since a few of the blood group paradoxers are out-

† From the Office of the Chief Medical Examiner of New York City and the Division of Immunohematology of the Jewish Hospital of Brooklyn.

* This quotation, as well as most of the others in this article, is taken from Augustus DeMorgan's *Budget of Paradoxes*, an entertaining and informative book, which was the inspiration for the title of the present article.

standing workers who have made important and even fundamental scientific contributions, the author has no intention of belittling or detracting from their position in science; indeed, he has the greatest respect for them and their accomplishments. But as Thomas Edwards (cited by DeMorgan) has pointed out, 'a man is unlearned who, be his other knowledge what it may, does not understand the subject he writes about'. Among the blood group paradoxers are leaders in the field of genetics and biometrics, but for insight into the nature of the Rh–Hr agglutinogens a knowledge of fundamentals of immunology rather than of χ^2 is essential. The foundations were laid by Karl Landsteiner and it is significant that blood group paradoxers hardly ever quote his basic work or, when they refer to Landsteiner at all, they often misquote or misconstrue his writings. The basic fallacious premise responsible for the predicament of blood group paradoxers is the tacit assumption of a 1 : 1 correspondence between antigen and antibody.† From this false premise the C–D–E notations followed as a natural sequel.

Reference may first be made to the recent article by E. B. Ford, an outstanding geneticist[6] who has devised a completely new notation for all blood group systems, including Rh–Hr. The nature of this notation is indicated in part by the footnote to Table 1. The ideas presented in this article were anticipated in 1953 by Wiener,[17] who pointed out that if the unnecessarily cumbersome but widely used symbolisms for the *Duffy* and *Kidd* types were applied for the sake of consistency also to the A–B–O, M–N, and Rh–Hr types, an unusable, ludicrous terminology would result. Wiener never dreamed, however, that any sensible worker would consider such an absurd idea seriously and actually suggest that such a terminology be used, as Ford has done.

The first article in the current issue of *Annals of Eugenics* (1955) is on blood groups and disease, not directly related to the subject at hand, except that it is another blood group paradox.* In the same issue are many articles on the Rh–Hr types. Attention may be called to 3 short articles on the distribution of the blood groups in different Jewish populations. The authors of these papers, following the lead of British investigators, give a table of Rh–Hr reactions as follows: C+D+E+c+ followed by the 'probable genotype' CDe/cDE, and next by the symbol R_1R_2, etc. The paradox is

† Carrying this fallacious premise to its logical conclusion, Pollak in his book on blood grouping (itself a veritable budget of paradoxes), when describing the subgroups of A and AB writes, '*eight antibodies are known:* anti-A_1, anti-A_1B, anti-A_2, anti-A_2B, anti-A_3, anti-A_3B, anti-A_4, and anti-A_4B.' In his book on clinical hematology, Dacie writes 'Group A_1 is probably of genotype AA_1 and A_2 of genotype AO.'

* The recent preoccupation of British investigators with studies on the distribution of blood groups in disease betrays lack of familiarity with the past history of blood grouping, and is responsible for another budget of paradoxes. These studies revive a line of investigation abandoned as irrational and unproductive more than 20 years ago, when articles on the distribution of the A–B–O groups in disease were in vogue (*cf.* Wiener, 1943). Consultation of the older literature will disclose numerous articles on topics such as blood groups in malaria, typhoid fever, hemophilia, dental caries, various mental diseases, longevity, etc.

that the symbol Rh_1Rh_2 (or R_1R_2) was originally devised as an abbreviation for $\mathbf{Rh_0}+\mathbf{rh'}+\mathbf{rh''}+$, before the letters C, D and E had been introduced by British workers, and so R_1R_2 is not 'shorthand' for the C–D–E symbols. Lack of insight into the subject is betrayed by the claim in the same article to have found 14 individuals of the very rare type Rh_2Rh_1 among 129 in one series, and 6 Rh_2Rh_1 among 200 in a second. That both the authors and editors failed to comment on this curious circumstance is highly significant.

In other articles in the same issue, the same paradox reappears. One pair of authors refers to the Rh–Hr symbols as the 'British short symbols' for the cumbersome CDE notations. This erroneous statement has been widely propagated in the literature, even though symbols such as R_1r, $R'r$, R_2r, etc., are really Wiener's 1944 nomenclature for the Rh–Hr phenotypes without the 'h'. In this same article, based on tests on only a few thousand persons, probabilities are reported to 6 significant figures.* One final example may be cited from a large Table in another paper in the same issue, and this one speaks for itself: 'Key to phenotypes: R_1r=D+C+C^w−c+E−e+; most likely genotype CDe/cde or CDe/cDe'.†

Analysis of Evidence

Part of the confusion existing among workers is caused by failure to recognize the various levels at which the Rh–Hr types must be discussed. Therefore Table 1, which compares the Fisher-Race and Wiener nomenclatures, has been divided into 6 sections dealing with antibodies, blood factors, genes, agglutinogens, genotypes and phenotypes.

Blood Factors and Agglutinogens

In Wiener's *Rh–Hr Syllabus*, the difference between a blood factor and an agglutinogen is pointed out. An agglutinogen is a substance in the discoplasm of the red cell, while blood factors are those attributes of the surface of the agglutinogen molecule which enable the agglutinogen to combine with its specific antibodies. In general, each agglutinogen has multiple blood factors, as shown by the fact that several antibodies of different specificities can react with the same agglutinogen (*cf.* Wiener and Wexler[21]).

British investigators, on the other hand, use the term agglutinogen and blood factor interchangeably, making the tacit assumption that each agglutinogen has but a single corresponding antibody. This fallacious premise is the entire basis of the C–D–E notations, and has led to multiple paradoxes, of which only one will be cited here as an example. When a human subject

*At any rate, this is more modest than previous papers where gene frequencies were reported to 7 significant figures.

† This entire line of symbols takes the place of the simple symbol Rh_1rh of the International Rh–Hr nomenclature—this, no doubt, is the paradoxers' concept of a 'simplification' of terminology.

of group O or an experimental animal is injected with group A blood, antibodies are frequently produced which are reactive not only with group A blood, but also with group B blood. This is readily explained by the fact that agglutinogens A and B have in common the blood factor **C** and the antisera in question contain the corresponding antibody anti-**C**. Since the fact that agglutinogens A and B have more than one blood factor is incompatible with their premise of a 1 : 1 correspondence between antigen and antibody, British investigators attempt to explain this phenomenon by postulating linkage of antibodies, as indicated by their designation anti-A+B. In other words, they assert that the injection of an antigen A stimulates not only the production of anti-A, but also an antibody for a different agglutinogen, anti-B, and that somehow these two antibodies fuse together. The same fallacious type of reasoning carried over to the Rh–Hr system has led to such symbolisms as anti-C+C^{w}, anti-D+D^{u}, anti-C+C^{u}+C^{v}+C^{w}, etc. (*cf.* Table 1).

Note that to emphasize the distinction between agglutinogens and their serological attributes, their blood factors, regular type is used to represent agglutinogens while boldface type is used for blood factors and their corresponding antibodies.

Cross-over Hypothesis

As long ago as 1942 it was shown by Wiener that the distribution of the **rh′** factor in the general population is not independent of the distribution of the **Rh$_0$** factor; and later the same was found to be true for factor **rh″**. This rules out the possibility that there are separate gene pairs, either loosely linked or independent, for factors **Rh$_0$**, **rh′**, and **rh″**, respectively. However, in 1944, the theory of linked genes was revived by Fisher and Race, who postulated that linkage was so close and crossing over so rare, that this accounted for the lack of random distribution of the three Rh factors with respect to one another. (The failure to observe crossing over in family studies has also been attributed to the presumed extremely low frequency of crossing over). Moreover, Fisher applied this concept to account for the low incidence of genes R^0, r', r'', R^z, and r^y, among white individuals in England as follows: According to Fisher and Race[5] the 5 rarer 'chromosomes' arose from the 3 more common 'chromosomes' by crossing over. Thus, from the common genotype DCe/dce (R^1r), by crossing over, the 'chromosomes' Dce (R^0) and dCe (r') are supposed to have arisen. Applying the same reasoning to the common genotypes R^2r and R^1R^2, Fisher and Race derived the equation $R^0=r'+r''+R^z$, and showed that this relationship among these 4 gene frequencies held for a particular series of British subjects tested for the Rh–Hr types. To explain the still lower incidence of 'chromosome' r^y, Fisher asserted that this 'chromosome' could have arisen only by crossing over from one of the rarer genotypes such as

Table 1: Nomenclature of the Rh–Hr Blood Types

Antibodies				*Blood factors*			*Alleles*	
Wiener	Fisher-Race			Wiener	Fisher-Race		Wiener	Fisher-Race*
	(a) Original Fisher	(b) Cappell (modernized)	(c) Ford		Race and Sanger	Ford		
Anti-**Rh$_0$**	*Δ*	Anti-D (Anti-D+D^u)	Anti-D^A	**Rh$_0$**	D	D^A	*r*	dcef
Anti-**rh′**	*Γ*	Anti-C (Anti-C+C^w)	Anti-C^A	**ℜh$_0$**	D^u	—	*r′*	dCeF
Anti-**rh^w**	—	Anti-C^w	Anti-C^W	**rh′**	C	C^A	*r′^{w}*	dC^{w}eF
Anti-**rh″**	*H*	Anti-E	Anti-E^A	**rh^w**	C^w	C^W	*r″*	dcEF
Anti-**Hr$_0$** (hypothetical) ..	*δ*	Anti-d	—	**rh(′)**	C^u	—	*r^y*	dCEF
Anti-**hr′**	*γ*	Anti-c	Anti-C^B	**rh***	E	E^A	*R^0*	Dcef
Anti-**hr″**	*η*	Anti-e	Anti-E^B	**rh^w**	E^w	—	*R^1*	DCeF
Anti-**hr**	—	Anti-f	Anti-F^A	**rh(″)**	E^u	—	*R^{1w}*	DC^{w}eF
Anti-**rh** (hypothetical) ..	—	Anti-F	—	**rh**	F	—	*R^2*	DcEF
				Hr$_0$	d	—	*R^z*	DCEF
				hr′	c	C^B	**ℜ^0**	D^{u}cef
				hr″	e	E^B	**ℜ^1**	D^{u}CeF
				hr	f	F^A	**ℜ^2**	D^{u}cEF
							ℜ^z	D^{u}CEF
							R^{ou}	DC– –
							R^{ox}	D– – –
							etc.	etc.

* To conserve space, the Ford symbols are omitted. For example, type Rh$_1$rh becomes C(A+B+), D(A+), E(A−B+), F(A+).

Table 1: Nomenclature of the Rh–Hr Blood Types—*Continued*

Agglutinogens		*Some Common Genotypes*		Designations of 12 Phenotypes Distinguished by Sera anti-**Rh_0**, anti-**rh′**, anti-**rh″**, and anti-**hr′**				
Wiener	Fisher-Race* (Agglutinogen quadruplets)	Wiener	Fisher-Race*	Wiener	Fisher-Race*			
					(a)	(b)	(c) Most likely genotype	(d) 'Shorthand' notations
rh	dcef	*rr*	dcef/dcef	rh	D−C−E−c+	ccde	cde/cde	rr
rh′	dCeF	*r′r*	dCeF/dcef	rh′rh	D−C+E−c+	Ccde	Cde/cde	R′r
rh^{w}	$dC^{w}eF$	*r″r*	dcEF/dcef	rh′rh′	D−C+E−c−	CCde	Cde/Cde	R′R′
rh″	dcEF	$R^{0}R^{0}$	Dcef/Dcef	rh″	D−C−E+c+	ccdE	cdE/cde	R″r
rh_y	dCEF	$R^{0}r$	Dcef/dcef	rh′rh″	D−C+E+c+	CcdE	Cde/cdE	R′R″
Rh_0	Dcef	$R^{1}r$	DCeF/dcef	rh_yrh'	D−C+E+c−	CCdE	CdE/Cde	R_yR'
Rh_1	DCeF	$R^{1w}r$	$DC^{w}eF$/dcef	Rh_0	D+C−E−c+	ccDe	cDe/cde	R_0r
Rh_1^{w}	$DC^{w}eF$	$R^{1}R^{1}$	DCeF/DCeF	Rh_1rh	D+C+E−c+	CcDe	CDe/cde	R_1r
Rh_2	DcEF	$R^{2}r$	DcEF/dcef	Rh_1Rh_1	D+C+E−c−	CCDe	CDe/CDe	R_1R_1
Rh_z	DCEF	$R^{2}r$	DCEF/dcef	Rh_2	D+C−E+c+	ccDE	cDE/cde	R_2r
$\mathfrak{R}h_0$	$D^{u}cef$	$\mathfrak{R}^{0}r$	$D^{u}cef$/dcef	Rh_1Rh_2	D+C+E+c+	CcDE	CDe/cDE	R_1R_2
$\mathfrak{R}h_1$	$D^{u}CeF$	etc.	etc.	Rh_2Rh_1	D+C+E+c−	CCDE	CDE/CDe	R_2R_1
$\mathfrak{R}h_2$	$D^{u}cEF$							
$\mathfrak{R}h_z$	$D^{u}CEF$							
Rh_0^{u}	DC− −							
Rh_0^{z}	D− − −							
etc.	etc.							

R^2r' or R^zr. Moreover, from the ratio of the frequency of the postulated cross-over 'chromosomes' to the frequency of the genotype from which they were said to have arisen, Fisher and Race concluded that the supposed closely linked Rh–Hr genes had the arrangement DCE. However, in these calculations, no allowance was made for the existence of $\mathbf{Rh_0}$ variants, and by analyzing published studies on other populations Wiener[16] showed that the relationship held only very exceptionally. In fact, in the second edition of *Blood Groups in Man*, p. 171, Race and Sanger now admit that 'it does not seem unfair to say that anthropological results have been inconclusive.'

Mutation

Like other series of allelic genes, the numerous Rh–Hr genes probably arose as a result of a series of gene mutations. Differences in stability of the various genes of the Rh–Hr allelic series probably are at least partly responsible for the prevailing differences in frequencies of the genes, while the differences in distribution among Caucasoids, Negroids and Mongoloids are probably largely the accidental result of isolation. In Fig. 1 is given one possible scheme showing how the various Rh–Hr genes identified to date could have arisen from one another by mutation. If one assumes that R^1, R^2, and r were the 'original' Rh–Hr genes in Caucasoids, and that the other genes arose from these 3 by mutation (not necessarily in a single step), this could account for the lower frequency of genes R^0, r', r'', r^y, and R^z. In particular, gene r^y would be expected to have the lowest frequency, because it presumably had to arise by mutation from one of the less common genes r', r'', or R^z. Perusal of the figure shows that the mutation hypothesis explains the present distribution of the genes more satisfactorily than the crossover hypothesis, especially since the former is far more comprehensive in its scope and can readily be extended to include the findings on lower primates.

Among 161 pure Chippewa Indians, Matson *et al.*[9] computed the following distribution of the Rh–Hr genes, $R^1=0.315$; $R^2=0.527$; $R^0=0$; $R^z=.019$; $r'=0$; $r''=.079$; and $r=0$. These authors, who favor the cross-over hypothesis, remarked: 'As expected the high R^2... is accompanied by moderate values of r''.' This statement could follow from the concept of origin of allelic genes by mutation, but is hardly to be expected under the hypothesis of crossing over from linked gene pairs. Under the latter theory the gene r'' would have to arise by crossing over from genotype R^2r, which does not exist among Chippewa since gene r is absent. Similarly, by crossing over from genotype R^1R^2, one could expect genes R^z and R^0 to arise in equal numbers. Yet R^z is present in this population while R^0 is not. By applying a similar analysis to data on other populations, it has been found that although the serological data may occasionally fit the cross-over concept,

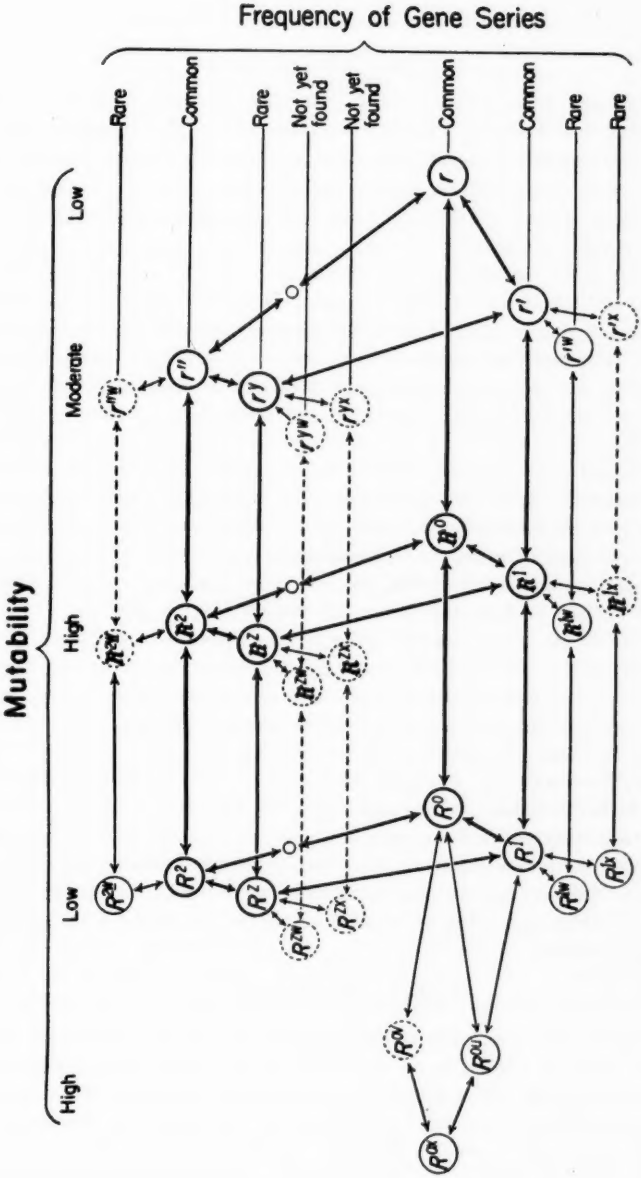
Frequency of Gene Series
Rare
Common
Rare
Not yet found
Not yet found
Common
Common
Rare
Rare
Mutability
Low
Moderate
High
Low
High

Fig. 1

it more often contradicts the hypothesis, while it is always in conformity with the hypothesis of mutation from multiple alleles.

Completely Linked Genes

More recently British investigators have been modifying the cross-over hypothesis to a theory of 'completely linked' genes. By adopting a theory of completely linked genes, British investigators concede the correctness of the theory of multiple alleles and the incorrectness of the cross-over hypothesis. Since a set of completely linked genes operates as a unit, the difference between completely linked genes and a unit gene or allele is purely one of semantics, and the supposed arrangement DCEF becomes meaningless. In fact, any series of alleles can be written in the form of completely linked genes, e.g. in place of the triple alleles *A*, *B*, and *O* for the A–B–O groups one could (like Furuhata) postulate completely linked gene couplets (*Ab*), (*aB*), and (*ab*), respectively; and, similarly, in place of the alleles *M* and *N* for the M–N types one could substitute the gene couplets (*Mn*) and (*mN*).

Significantly, the identical evidence that was originally offered by Wiener more than a decade ago for his theory of multiple alleles (namely, the sum of the gene frequencies, calculated by his square root formulae, totals 100%), and against the theory of linked genes (namely, the lack of randomness in distribution of factors **Rh_0**, **rh′**, and **rh″** with respect to one another), are now offered by Race and Sanger (cf. *Blood Groups in Man*, pp. 114 and 173) as evidence supporting the concept of completely linked genes.

In fact, it is now argued by Levine and others that since the two hypotheses, complete linkage and multiple alleles, for practical purposes yield identical results, the nomenclature used is merely a matter of personal preference, so that each worker selects the terminology he finds 'simpler' for his purpose. However, the important differences between the views of Wiener and of Fisher and Race are not a genetic level, but on a serologic level, as has already been pointed out, and since the two nomenclatures interpret the same observations differently, they cannot both be correct. The C–D–E notations which are based on the incorrect concept of a 1 : 1 correspondence between antigen and antibody must therefore be discarded for the sake of scientific accuracy.

Fisher's Predictions

Much capital has been made of the supposed confirmation of certain predictions made by Fisher, as an argument for the linked gene hypothesis. When the existence of factor **hr′** (c) reciprocally related to **rh′** (C) was established, Fisher predicted the existence of two additional Hr factors, **Hr_0** (d) reciprocally related to **Rh_0** (D), and **hr″** (e) reciprocally related to **rh″** (E). This he asserted was based on the concept of triply linked gene

pairs, C–c, D–d, and E–e. At the outset it should be pointed out, however, that this very reasonable prediction has no direct bearing on the genetic theories, and fits at least equally well with Wiener's concept of the Rh–Hr agglutinogens. In fact, since blood factors are merely attributes of agglutinogens, no limit is set on the number of blood factors an agglutinogen may have, so that the number of blood factors is largely limited by one's enterprise and ingenuity in searching for and finding Rh–Hr antisera of new specificities.

Anti-**hr″** (e) serum was soon discovered by Mourant, and other examples were found by Wiener and others. Race and Fisher then published a paper in *Nature* proving mathematically that Levine's original anti-Hr serum was anti-$\mathbf{Hr_0}$ (d)[23]. No further reference is made by them to this early paper, now that it is generally recognized that Levine's serum really has the specificity anti-**hr′** (c). Later, two or three reports appeared claiming the discovery of anti-$\mathbf{Hr_0}$ (d), notably the one by Haberman and Hill, which has been cited a good deal, especially by Fisher[4], and is described in detail by Race and Sanger in their book (*Blood Groups in Man*, 1954, pp. 129–130, and Table 38 on p. 117) as evidence supporting the Fisher-Race hypothesis. Wiener tested Haberman and Hill's serum, but could not confirm the presence in it of anti-$\mathbf{Hr_0}$ (d)—only anti-**hr′** (c). Presumably, this serum had also been previously tested by other workers in the field who could not confirm the report, though no mention is made of this in Race and Sanger's book. However, on p. 181 of the book appears the statement: 'Now that anti-f is commonly found in anti-c serum, we feel doubtful about the identity of those two examples of anti-d'. Thus, of the two antisera predicted by Fisher only one (anti-**hr″**) has actually been found, and instead of anti-$\mathbf{Hr_0}$ a different serum anti-**hr** (f) has recently been found, as well as other Rh–Hr antisera, notably anti-$\mathbf{rh^w}$, not predicted by Fisher.

Fisher's prediction of two antisera is frequently cited by Race as a prediction of 22 'interactions'. These 22 'interactions' are merely the serologic properties of anti-**hr″** and anti-$\mathbf{Hr_0}$ sera which are to be expected by definition.* Thus, this is merely a change in scale calculated to impress the uninitiated, just as one might offer a child 25 pennies instead of a 25 cent piece. However, it is necessary to emphasize again that the question whether or not Fisher's prediction was correct has no bearing on the basic problem, since the essential difference between the two concepts is on a serologic level, viz. the difference between a blood factor and an agglutinogen.

'Deletions'

Since according to the Fisher-Race hypothesis the Rh–Hr factors are supposed to be inherited in sets of 3 (or 4 if one takes the newly postulated

* Thus, the number of interactions merely reflects the status of knowledge concerning the Rh–Hr series of allelic genes, so that at the present time as many as 20 interactions could be defined for each Rh–Hr antibody instead of only 11.

locus F–f into account), the discovery of the existence of individuals with blood containing the factor **Rh_0** alone was upsetting to them. This is readily explained by considering such individuals to be homozygous for a new gene R^{0x}, giving rise to a corresponding agglutinogen Rh_0^x having the blood factor **Rh_0**, but lacking the factors **rh′–hr′**, **rh″–hr″** and **hr**. To account for this type of blood Race felt the need to invoke the conception of deletion, and designated the blood as –D–. This conflicts with the observation that with only rare exceptions there must be at least one representative of each locus present for development to proceed normally. In Drosophila, for example, large deletions are lethal, while small deletions are viable only in heterozygous form. It is well established that deletions produce marked phenotypic modifications, yet all individuals encountered to date homozygous for the supposed deletion –D– have been entirely normal.

'Position Effect'

Let us consider blood of phenotype rh_yrh, which according to the multiple allele theory could arise from either of the two genotypes $r'r''$ or r^yr. The corresponding genotypes under the linked gene theory would be dCe/dcE and dCE/dce, respectively. It will be noted that under the latter hypothesis, in either genotype the following 6 genes are present dd, Cc, and Ee. Since the Fisher-Race hypothesis states that each gene produces a corresponding agglutinogen, the gene products should in both cases be identical. According to the multiple allele theory, on the other hand, genotype $r'r''$ would produce the 2 agglutinogens rh′ and rh″, while genotype r^yr would produce the 2 agglutinogens rh_y and rh. While anti-**rh′** serum cross-reacts with agglutinogens rh′ and rh_y, and anti-**rh″** serum cross-reacts with rh″ and rh_y, one could expect that with sufficiently refined technics a difference in behavior between the agglutinogens of each pair could be demonstrated with such antisera. Indeed, Race *et al.* found that with some, though not with all, anti-**rh′** and anti-**rh″** sera, blood from individuals of these 2 different genotypes could be distinguished. This phenomenon has been called by Race a pseudoallelic 'position effect', but merely applying a name to a phenomenon does not explain it.

Factor **hr** (f)

As has already been pointed out, the main limitation to the number of blood factors which characterize an Rh–Hr agglutinogen is the enterprise of investigators in searching for and finding antisera of new specificities. Thus, the recently discovered antiserum anti-**hr** (anti-f) readily fits into the scheme since it merely detects an additional factor shared by the agglutinogens determined by the genes r and R^0 and absent from the other Rh–Hr agglutinogens. Under the linked gene concept, it becomes necessary to invoke

the existence of a new pair of alleles F and f, and to modify the theory to one of quadruply linked gene pairs. Significantly, antibodies for the hypothetical factor F have not been found and it has been suggested by Race and Sanger that the 2 antisera that were at first thought to contain anti-$\mathbf{Hr_0}$ (anti-d) were actually examples of anti-**hr** (f). Thus, in the postulated structure of 4 pairs of linked genes, 2 of the more important buttresses d and F are lacking.

Phenotype Notations

The International Rh–Hr Nomenclature clearly distinguishes between blood factors, agglutinogens, genes and between genotypes and phenotypes. The failure of the C–D–E notations to distinguish among these clearly has led to ambiguities and errors and there has been considerable difficulty, especially in finding satisfactory designations for the phenotypes. For example, as was shown in Table 10 of Wiener's *Rh–Hr Syllabus*, corresponding to the phenotype Rh_1rh there are at least 25 different C–D–E symbols, of which only the 4 most important are given in Table 1. Since the proof of the pudding is in the eating, the fact that the C–D–E notations for the phenotypes have proved unsatisfactory in actual practice is a further reason, were any needed, for discarding them.

'Shorthand' Notations

Because the C–D–E notations have proved cumbersome, especially for oral use, and unsatisfactory for designating phenotypes, Fisher and Race have been compelled to have recourse to certain 'shorthand' symbols. As can be seen from Table 1, these shorthand symbols are nothing more than Wiener's Rh–Hr symbols of more than a decade ago without the 'h'. Significantly, the so-called shorthand symbols differ less from the symbols presently used by Wiener, than the numerous variations of the C–D–E notations for phenotypes differ from one another. Therefore, the following statement in Race and Sanger's book, p. 146, which has been copied many times in the literature, is the opposite of the truth: 'We have used both C–D–E and our (sic!) short symbols without change for 10 years. Dr. Wiener's notations have undergone changes every year, and we still feel no confidence that it has yet reached stability.'‡ Moreover, their objection that 'Dr. Wiener has been calling his notations the "International Nomenclature" ' is inconsistent with their own use of these notations under the transparent pseudonym of 'shorthand' notations. If their objection is sincere then they should also use the eponym 'Wiener nomenclature', because the term 'shorthand'

‡Wiener's notations have indeed undergone changes to correspond with advances in knowledge as new facts have been unearthed. C–D–E paradoxers, on the other hand, have resorted to distortion of facts in order to compel them to fit into their preconceived neat but incorrect concept of 3 factor pairs, D–d, C–c, and E–e.

notations is incorrect in implying that the Rh–Hr symbols are abbreviations of the British C–D–E notations.*

Another interesting paradox: C–D–E workers labor mightily with maximum likelihood calculations to extract the maximum information from data on the distribution of the Rh–Hr types, and report the calculated gene frequencies to 8 significant figures. At the same time, instead of phenotypes they report 'most likely genotypes' thus accepting errors greater than 10% without being disturbed.

Medico-Legal Applications

The inadequacy of the C–D–E notations is further demonstrated in the medico-legal applications of the Rh–Hr tests. Failure to adopt the International Nomenclature for phenotypes and genotypes, has led some British workers into numerous anomalies and difficulties which, from the medico-legal point of view, may easily bring Rh blood group tests into discredit in the courts. For example, on p. 124 of Race and Sanger's *Blood Groups in Man*, there appears the following: 'This phenotype group R_1r (++−) includes the genotypes R_1r, R_1R_0 and R_0R'...'.

This short statement exposes several paradoxes. In the first place, the same short notation (R_1r) has been employed for the phenotype Rh_1rh as for the genotype R^1r. Secondly, the sequence of + and − signs is entirely meaningless unless the order of serological reactions which they define is precisely indicated. In their attempt to bolster up their theory of linked genes, Fisher and Race have been led to alter the sequence of the individual loci of the genes on the chromosomes from CDEF to DCEF, with the result that phenotypes, genotypes and serological reactions are presently being expressed in the former sequence by some workers and in the latter by others. In the example quoted, the order of serological reactions indicated is C+c+D+E−, which corresponds to neither of the above. Finally, the use of the same notation indiscriminately for phenotypes and genotypes as the occasion demands, has led to the malposition of the numerals 1 and 0 in the genotypes.

Writing the above statement in the International Nomenclature it would read simply and correctly: The phenotype Rh_1rh includes the genotypes R^1r, R^1R^0 and R^0r'. That this confused misuse of the British shorthand notations may have serious medico-legal repercussion is shown in Table 2 where the matings in Race and Sanger's Table were defined by the antisera anti-C, –c, –D, –E.

From the British authors' Table, it might be inferred that a type $Rh_1^{\text{w}}rh$

* To deny the true origin of symbols such as R_1r is as misleading as, when using R.S.V.P. to mean 'please reply', to deny the origin of this abbreviation from the French '*répondez s'il vous plait*'.

child could result from a mating of $Rh_0 \times Rh_1rh$ parents, unless it is appreciated that the peculiar domestic convention of the authors in respect of this Table is to include the reaction of anti-**rh**^{w} with anti-**rh**′ in the serological reactions whereby the filial relationships are established.

Table 2: Comparison of Rh–Hr and C–D–E Nomenclature (Sample Mating)

Nomenclature	Parents	*Children Possible*
International Rh–Hr Nomenclature*	$Rh_0 \times Rh_1rh$	rh rh′rh Rh_0 Rh_1rh
British C–D–E Notations†	cDe/cde, cDe/cDe × CDe/cde, CDe/cDe, Cde/cDe	cde/cde Cde/cde cDe/cde, cDe/cDe CDe/cde, CDe/cDe, Cde/cDe
British 'shorthand' Notations§	$R_0r \times R_1r$; R_0R_0; R_1R_0, R_1^wr, $R_1^wR_0$, R_0R', R'^wR_0	rr $R'r$ R_0r R_1r; R'^wr R_0R_0 R_1R_0, R_1^wr, $R_1^wR_0$, R_0R', R'^wR_0

* This is mating no. 128, page 342, in the book *Rh–Hr Blood Types* by Wiener, 1954.
† Mating no. 27, page 312, in the book *Blood Transfusion* by Keynes, 1949.
§ See p. 325, in the book *Blood Groups in Man*, by Race and Sanger, 2nd edition, 1954.

The matings in Race and Sanger's Table were defined by the antisera anti-C, -c, -D, -E.

The presence of the factor **rh**^{w} can only be determined with a specific anti-**rh**^{w} serum, which does not react with **rh**′.

Another example from this Table could lead to the incorrect inference that children of type Rh_1rh are possible from the mating $Rh_0 \times Rh_1^wrh$.

The way these 2 matings have been combined in the book of Race and Sanger, if not incorrect or meaningless, is certainly misleading.* At any rate, the use by workers in the field of such cumbersome and confusing C–D–E symbolisms cannot help but shake the confidence of lawyers and judges in these valuable blood tests. This is another reason, if any were needed, for the exclusive use of the international Rh–Hr nomenclature.

* This is as illogical and confusing as to prepare a heredity table for the A–B–O groups, excluding tests for the subgroups of A, but giving mating

$$A \times AB \rightarrow A, B, AB \quad \text{as} \quad \begin{Bmatrix} A_1 \\ A_2 \end{Bmatrix} \times \begin{Bmatrix} A_1B \\ A_2B \end{Bmatrix} \rightarrow \begin{Bmatrix} A_1, \\ A_2 \end{Bmatrix} B, \begin{Bmatrix} A_1B \\ A_2B \end{Bmatrix}$$

Anthropological Applications

Further evidence of the inadequacy of the C–D–E notations is provided in the anthropological application. In his book, *Distribution of the Human Blood Groups*, Mourant has compiled a mass of valuable data published during the decade following the discovery of the Rh factor. Unfortunately, the data regarding the Rh–Hr types is spread among 13 different complex Tables, making it difficult to locate and interpret the data on any specific population. As Wiener has shown, by the use of the International Rh–Hr Nomenclature, these 13 Tables can be combined into a single compact Table, in which all the data can be presented logically and clearly, thus making the information much more accessible.

Clinical Applications

The inadequacies of the C–D–E notations have their most serious implications in the clinical application of the Rh–Hr tests. This is due to the failure to indicate the special position of the **Rh_0** factor. For example, there is nothing about any of the numerous C–D–E equivalents for type rh′rh, viz. Ccde or Cde/cde or (+ + − − −), or Ford's recent designation C(A+B+) D(A−), E(A−B+), F(A+), to indicate clearly that such an individual is **Rh_0** negative, so that if he requires a blood transfusion he should be given only Rh-negative blood.* If the type rh′ individual in question is an expectant mother, tests for **Rh_0** antibodies are indicated provided the husband is Rh positive, but there is nothing about any of the multiple C–D–E designations in use for this type to indicate that fact. The C–D–E notations are even more confusing in the case of type Rh_1Rh_1 individuals who become sensitized to the **hr′** factor. Since at the author's laboratory the C–D–E notations are never used (only the Rh–Hr nomenclature) the author is uncertain how such problems are managed in laboratories where the C–D–E notations are used.

Supposed Advantages of the C–D–E Notations†

After reading the foregoing discussion, the intelligent reader will wonder what are the supposed advantages of the C–D–E notation which are re-

* In the International Nomenclature the **Rh_0**-negative types, rh, rh′, rh″, rh_y, are clearly distinguished from the **Rh_0**-positive types, Rh_0, Rh_1, Rh_2, Rh_z by the small 'r' and capital 'R', respectively. On the other hand, to the uninitiated, there is nothing to indicate which of the 3 factors C, D or E is most important clinically.

† It has generally been overlooked that the idea to use simple letters for the Rh–Hr factors was not original with Fisher or Race, since in 1943 Wiener used the letter U for factor **rh′**, and the letter V for **rh″**. It will be noted that Wiener carefully avoided the use of the letters C–D–E for two reasons, firstly, in order to avoid the false implication of any relationship to the A–B–O system, and secondly, because as experienced workers in the field were all aware, the letter C was being used already for a factor of the A–B–O system. (Obviously, the recent charge by C–D–E paradoxers that Wiener coined the symbol C for a factor of the A–B–O system merely to embarrass them is just false propaganda, since this use of the symbol C antedates the discovery of Rh). Wiener abandoned the use of simple literal symbols, because by their use it was not possible to distinguish properly between blood factors and agglutinogens.

sponsible for its wide popularity. According to Race, the advantage of the C–D–E notations is their simplicity, since, according to him, the C–D–E symbols clearly indicate which agglutinogens are present in a particular blood specimen. This may be true of designations such as C+C^{w}−c+ D+E−,† but such elaborate symbols are hardly ever used in practice, and the statement certainly is not true for the C–D–E notations used by Race himself in his own book. For example, the symbols (+++−) or CDe/cde which he uses for type Rh_1rh, do not 'clearly indicate' the agglutinogens present in a specimen of blood. To mention only one point, the symbol 'little e' is sometimes used to represent the absence of factor **rh″**, and at other times to indicate the presence of factor **hr″**, and similarly for 'little c'. Moreover, the C–D–E equivalent for type rh′^{w}, namely, C^{w}deF is completely misleading, since as Stormont has pointed out, it conveniently omits the symbol for factor C (**rh′**) present in such blood, but includes the symbols for 2 hypothetical factors, d and F, for which no tests have been made and, in fact, for which no antisera are available.

The assertion that the C–D–E symbols are self-explanatory is not only untrue but is based on a fallacious premise. In no science are the specialized symbols designed merely to be intelligible to beginners or those not working in the field. Instead they are intended for the convenience and use of experts. It is up to the beginner to learn the meaning and use of the symbols peculiar to a science in which he is interested, rather than for scientists and technical journals to bring their articles down to the level of persons who do not know the subject. Since every neophyte is permitted to devise his own notations for the Rh–Hr types, using the letters C, D and E, it is no wonder that there are more than 25 C–D–E notations for the same Rh–Hr type. This appeals to the beginner because it is so much easier to be careless and inexact than to be precise; in science, there is room for only the single correct description of each natural phenomenon, but the careless worker will find it simpler to use any one of an infinite number of incorrect descriptions. The worker who finds it too exacting to find the correct answer, is delighted when the endorsement of leading investigators makes it respectable to be careless and inaccurate.

The other supposed advantage of the C–D–E notations, that the symbols completely describe the serological reactions of the blood, besides being untrue, is also based on a fallacious premise. In no branch of science do the symbols pretend to describe fully the substances they represent, but are intended merely for purposes of identification. This was true also in the blood grouping field before the C–D–E symbols were introduced; for example, there is nothing in the symbol 'group O' to indicate the presence of anti-A and anti-B in the serum, or in the symbols for the subgroups

† For the beginner who finds it easier to have all the reactions spelled out, it would be wiser to start immediately on the right foot by doing this as follows: **Rh_0**+, **rh′**+, **rh^{w}** −, **rh″**−, **hr′**+. Then, as he becomes more familiar with the subject this can readily be abbreviated to Rh_1rh.

A_1 and A_2 to indicate their complex serological properties. Even were it possible to include everything known about a substance in its name or symbol, this would be undesirable, because the symbol would have to be changed and would become more and more cumbersome with each new discovery. To cite only one example: following the discovery of **hr** (f) factor, British investigators found it necessary to change their symbols for the 'chromosomes' to cdef, CdeF, cdEF, etc., whereas the International Nomenclature for the Rh–Hr genes remained unchanged as *r*, *r'*, *r''*, etc.

If the C–D–E notations were really satisfactory, there would be no need for Fisher and Race to resort to the 'shorthand notations' which are merely Wiener's 1944 Rh–Hr symbols without the 'h'. Race writes and talks of types R_2r, rr, etc., diagnosed with antisera, anti-C, anti-D, etc., thus producing a hybrid of 2 incompatible nomenclatures. Moreover, it is inconsistent to retain the 1944 Rh–Hr symbols without making any necessary revisions, while at the same time introducing multiple changes in the C–D–E notations. In fact, by failing to use the capital R exclusively for Rh-positive individuals, one runs the risk of confusing types R'r and R_1r (correctly designated rh'rh and Rh_1rh, respectively). Moreover, failure to distinguish phenotypes and genotypes when using their (sic!) 'shorthand' notations, has caused British workers to make many errors in the past, and will continue to be a source of mistakes.

Since enough information is now available to resolve the Rh–Hr problem, especially with regard to nomenclature, Wiener suggested the formation of a fact-finding committee to review the present status of the subject. Because more than 7 years had passed since the report was published in *Science*,* plans were made for a new meeting by the Subcommittee on Blood Grouping Tests of the Committee on Medico-legal Problems of the American Medical Association. The plans for the meeting were abandoned when Fisher and Race declined an invitation to participate. It now appears doubtful whether such a meeting will ever be held†.

Every new scientific discovery and theory is said to go through 3 stages. In the first stage, the discovery is said to be incorrect. When the validity of the discovery can no longer be denied, it is said to be unimportant. Finally when the importance of the discovery becomes obvious to all, it is said that it is not new. Not so long ago Wiener's multiple allele theory was criticized as incorrect, and his observations regarding the difference between Rh–Hr blood factors and agglutinogens were completely disregarded. Today, it is admitted that this work is correct, but it is argued that it is unimportant, since 'completely linked genes' yield the 'same' results for

* The conclusions and recommendations in the *Science* article have been superseded by a statement published in the Journal of the American Medical Association[11]. This statement was submitted to R. R. Race before publication for his criticism. He made none, nor have C–D–E paradoxers commented on this more up to date statement since its publication.

† This article contains some of the material the author would have presented at the meeting.

practical purposes. It can be visualized that within the very near future, workers will gradually drop the C–D–E notations, but then it will be stated that Wiener's Rh–Hr nomenclature is not original with him, since, as Race and Sanger assert, they have been using their (sic!) 'shorthand' notations 'without change for 10 years'.

Conclusions

Any reader who has read the foregoing with an open mind, and has sufficient scientific background to understand the evidence which has been presented, will have no difficulty in ascertaining the facts regarding Rh–Hr serology, genetics and nomenclature. To him it will be clear that the use of the letters C–D–E–F for the Rh–Hr types is based entirely on a false serological premise which has led to paradoxes in the past and will continue to do so in the future. He will understand why the C–D–E–F notations must be discarded, and the International Rh–Hr Nomenclature used exclusively for reporting observations regarding these blood types.

It is hoped that the same outstanding geneticists and biometricians, who through lack of prior knowledge of blood group serology fell into the C–D–E fallacy, will lead the way in correcting the paradoxes for which this has been responsible. According to a quotation from Galton which appears in every issue of the *Annals of Eugenics*, 'it is a triumph of scientific men . . . to feel sufficiently masters of themselves to discard contemptuously what may be found untrue'. The statement often repeated that there is still not enough evidence to settle the problem is merely another way of saying that the one making this assertion has not been personally convinced.

It must be emphasized once more that no personal criticism is intended by anything written in this review. As already mentioned, I have the highest regard for the ability and contributions of many of the investigators whose work on Rh–Hr serology and nomenclature it has been necessary to criticize. What is important in science is not who is right, but what is right; and every investigator has the duty not only to point out what is right but to expose what is wrong. Only in that way can progress of knowledge and understanding be fostered and that is why this article had to be written. Since all human beings are fallible, the reader may possibly detect some minor flaws* in the presentation of the evidence, and one may anticipate

* In 1949, tests on 145 individuals having agglutinogen rh′ showed none with the factor **rh^w**, and the present author erroneously used this fact as an argument against the theory of triply linked genes. On p. 138 of *Blood Groups and Man*, 2nd edition, Race and Sanger make capital of this slip, which is irrelevant to the main issue. On the other hand, nowhere in the book do they refer to the important evidence which has been advanced pointing out the paradoxes to which their erroneous viewpoint has led. Incidentally, in 1954 Wiener reported a type rh′^{w} woman who was sensitized to the **Rh$_0$** factor (Wiener, 1954) and more recently he has found the rare rh′^{w} agglutinogen in a father and child (unpublished observation). Race and Sanger also blame Wiener for questioning reports claiming the discovery of anti-**Hr$_0$** (anti-d), and they cite these reports in great detail in their book and use this as evidence in support of their viewpoint. Yet, in another part of the same book they confess their own doubts concerning the reliability of these observations.

that blood group paradoxers would make capital of any error, no matter how trivial or irrelevant to the main argument. However, this possibility causes the writer no concern, because the facts are clear and unchangeable by anything that anyone might say or write. If any reader finds the manner chosen by the present author to present the evidence objectionable in any way, he should charge this against the writer and not let his personal feelings blind him to the facts.

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Identification of the Kell Factor

In Dried Blood Stains*

A Case Report

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and

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In a case of homicide the alleged assailant claimed, when apprehended, that her victim had brutally assaulted her and that she had struck him with a knife in the chest in retaliation for his assault. In support of her story she directed attention to the front of her dress which was stained with blood. She maintained that these blood stains had come from her own injuries, mainly from a copious nose bleed following a blow in the face. The Police Department had assumed that these stains came from the wound of her victim who had bled profusely from an incised wound of the aorta. In order to test the veracity of the woman's story the following specimens were submitted for an attempt to be made to define the origin of the stains:

1. Whole blood (autopsy heart puncture sample) from the victim.
2. Whole blood from the assailant.
3. The blood-stained dress from the assailant.
4. The blood-stained shirt of the victim.
5. A butcher-type kitchen knife with dried blood stains on the blade.

All the specimens were 3 days old when received.

Procedures and Results

1. *Blood Typing.* The whole blood specimens (1 and 2) were typed in duplicate by independent workers with the results shown in Table 1. It will be seen that there was no difference in respect of the ABO or Rh

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systems. In the MNS system the victim's blood contains the S antigen while the assailant's blood lacked it. There were also differences in the Kell, Duffy, and Lewis systems, specimen No. 1 being K-positive and Fya-positive and Leb-positive while specimen No. 2 was K-negative, Fya-negative and Lea-positive.

Table 1: The Results of Typing Whole Blood Specimens from Victim and Assailant

Specimen	*Antiserum*														
Origin	A	B	C	C^w	D	E	c	M	N	S	K	Fy^a	Le^a	Le^b	P
1. Victim	+	0	+	0	+	0	+	+	+	+	+	+	0	+	+
2. Assailant	+	0	+	0	+	0	+	+	+	0	0	0	+	0	+

+ = a positive reaction
0 = a negative reaction

It was decided to attempt identification of the stain on the basis of the Kell antigen.[1] The Lewis system was not regarded as suitable to work with because of the lability of the antigen. Previous experience with the S and Duffy systems suggested that they would be unlikely to survive drying. In routine typing of whole blood, S and Fya reactions are known to be less satisfactory with older samples while Kell reactions are known to be much less dependent on the age of the specimen.

2. *Kell Typing of the Stained Clothing.* Pieces of cloth about 1 inch square were cut from the shirt of the victim (specimen 4) and from the dress of the assailant (specimen 3), each piece being chosen to resemble the other as closely as possible in intensity of blood staining. Similar areas of unstained cloth from each garment were taken as negative controls and yet other pieces were cut and deliberately stained with known Kell-positive and known Kell-negative blood. These latter pieces were air-dried for 2 hours at 30° C. Each of the 8 portions was finely shredded with scissors before being placed in a test tube and to each tube was added 0.2 ml. of a 1 : 5 saline dilution of a potent anti-Kell typing serum. The tubes were then incubated for 1 hour at 37° C. with frequent shaking. After the completion of incubation all tubes were centrifuged and as much as possible of the supernatant anti-Kell serum was removed from each and placed in a dry tube. Aliquots of 0.05 ml. of each supernate were then separately incubated for 30 minutes at 37° C. with an equal volume of a 2% suspension of Kell-positive and Kell-negative red cells. Finally, anti-globulin (Coombs) tests were performed on all 16 tubes and the results expressed as in Table 2.

It can be seen from Table 2 that complete removal of anti-Kell activity was obtained by treating the diluted anti-Kell serum with the blood-stained cloth from the victim's shirt and also with the cloth from either shirt or

Table 2: Results of Absorption Test of Various Samples of Cloth for Kell Antigen. Absence of Agglutination Shown in the final Column Shows the Presence of the Kell Antigen in the Material Tested.

Material	*Kell Type of Stain*	*Reaction of Supernate with Cells*	
		K-Negative	*K-Positive*
Shirt	Unknown	0	0
Dress	Unknown	0	+++
Shirt	Unstained	0	+++
Dress	Unstained	0	+++
Shirt	K-positive	0	0
	K-negative	0	+++
Dress	K-positive	0	0
	K-negative	0	+++

+++ indicates strong agglutination by antiglobulin test.
0 indicates no agglutination by antiglobulin test.

dress which had been deliberately stained with Kell-positive blood. The original stained cloth from the assailant's dress failed to absorb the anti-Kell antibody. A similar failure was also shown by the unstained cloth from either garment and by the specimens which had been deliberately stained with Kell-negative blood. Therefore the blood stains on the victim's shirt may be said to come from the victim (or some other Kell-positive person). The blood stains on the assailant's dress could not possibly have come from the victim.

Portions of the deliberately stained cloth of both garments were retained at room temperature for a further 3 days and an absorption test similar to that described above was carried out on them. This test gave results consistent with the 3-day-old dried blood, being capable of absorbing specific antibody from the anti-Kell typing serum.

3. *Kell Typing of Bloodstains on the Knife Blade.* A test, essentially similar to that used for typing the blood-stained garments, was set up on the dry material scraped from the blade of the knife (specimen 5). As controls, Kell-positive and Kell-negative bloods were deliberately dried on another knife blade; an approximately similar quantity of each material was placed in 3 tubes together with diluted anti-Kell reagent. After incubation, the supernatant serum was tested with Kell-positive and Kell-negative red cells as described above; the results are shown in Table 3.

The results of this test were manifestly not as satisfactory as those of the tests on the garments. The weak agglutination noted in the tube containing anti-Kell which had been treated with material from the knife precludes a definite statement that these stains were of Kell-positive blood. However, the results might be classified as 'extremely suggestive but not conclusive'. The test could only be regarded as definitive if the cells in this tube had been either strongly agglutinated (therefore a Kell-negative stain) or not at all agglutinated (therefore a Kell-positive stain).

Table 3: Results of an Attempt to Detect the Kell Antigen in Scrapings from the blade of a Knife. (Interpretation as in Table 2.)

Material	*Kell Type of Stain*	*Reaction of Supernate with Cells*	
		K-Negative	*K-Positive*
Scrapings from alleged weapon	Unknown	0	+
Simulated Scrapings	K-positive	0	+
	K-negative	0	++++

Discussion

The absorption method for detecting an antigen is a well-recognized immunologic technique. It depends upon the specific diversion or neutralization of an antibody by an antigen and is usually employed when the antigen in question is in a physical state which does not permit direct observation of an antigen-antibody combination. Provided adequate controls are used, the conclusions which may be drawn from a neutralization test are quite valid. Perhaps the best known application of a neutralization test (in relation to blood groups) is in defining the presence or absence of A or B group specific substance in saliva or other body fluids. It may also be applied readily to the determination of the A or B groups of dried blood smears.[2]

Experience with the lability of some of the iso-antigens of human erythrocytes has led to a general failure of appreciation of the possibilities of using the more recently discovered red cell antigens for identifying blood stains by the absorption technique.

The present case is cited as an instance of the successful use of one of these 'newer antigens' in a problem of stain identification and would suggest the advisability, in a similar situation, of attempting to exploit whatever blood factors may be thought to be present in a dried stain or otherwise denatured blood specimen.

Summary

The problem of the identification of human dried blood stains was solved by using the specific neutralizing power of the Kell antigen present in one of them.

A description is given of the method employed to demonstrate the Kell antigen in a portion of blood-stained clothing.

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Medico-Legal Problems in Blood Grouping

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Since January 1945 we have had occasion to examine several thousand dried blood stains as well as seminal stains and saliva stains.

We have confined our blood tests[1] to routine preliminary, confirmatory, precipitin, and ABO grouping. In exceptional cases a search was made for the factor M; but it was not always possible to conduct all these tests on a dried blood stain.

We were able to diagnose a human origin in about 85% of the stains examined; and we were able to diagnose the basic group in about 64% of the human blood stains identified.

Our experiences indicated that about 10% of the cases examined for blood identification eventually reached court. Wiener[2] (who also quotes Lewinski[3]) reports that in about 10% of the cases they examined the results were used. In the others the defendant and the victim belonged to the same group; or the unstained portions of the clothing gave the same specific reactions as the stain itself; or the stains gave no specific reactions at all because of deterioration.

Besides the identification of fresh blood, dried blood stains and other body fluids, the other highly important medico-legal application of blood grouping is in the exclusion of paternity.[4] We have had several paternity exclusion problems, one of which was an infanticide case.

Problems Encountered in Military and Civil Courts: Time after time one is asked in Court whether it is possible to distinguish between male and female blood; whether the blood stains on a certain garment are of menstrual origin; whether there are blood tests which would indicate racial origin; the approximate age of stains; and, more recently, whether a questioned blood stain could be of anthropoid origin.

We cannot as yet differentiate between blood of the male and female. But we can detect in menstrual blood stains elements highly suggestive of its origin. About 50—75% of the menstrual discharge consists of blood, the remainder being made up of mucosa and vaginal epithelium.[5] In the forensic medical literature there is little information about the identifica-

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tion of dried menstrual blood stains. Gordon, Turner and Price[6] hold that the demonstration of epithelial cells in blood stains on garments does not establish the menstrual origin of such stains, because worn clothing normally contains similar epithelial cells. They also state that there is no reliable method of distinguishing a menstrual blood stain from any other type of blood stain. Gonzalez, Vance, Helpern and Umber[7] hold that the demonstration of red brown iodophil cells in a dried blood stain is characteristic of menstrual blood. A positive iodophil reaction indicates that the epithelial cells store glycogen. Normal surface skin epithelial cells do not store glycogen whereas epithelial cells of the uterus do. For that reason we hold to the latter school of thought.

On numerous occasions intact spermatozoa admixed with menstrual blood have been identified on the fly region of trousers. On grouping such a blood stain it has been observed that the seminal stains interfered with the true group of the blood. This is undoubtedly due to the higher concentration of the group specific substance to be found in semen.

There are no definite blood tests, to my knowledge, which would indicate racial origin. The so-called sickle cell, while undoubtedly having considerable significance, could not be accepted as evidence in a criminal case. Manoiloff[8] of the Anthropological Institute at Leningrad did a great deal of work on the determination of racial origin from blood. He concentrated on making specific tests in order to differentiate between the blood of cattle and the blood of horses. He concludes that 'the species reaction on our material has given the possibility of distinguishing cattle from horses by their blood serum in 100% of the cases.' While this may be of academic value we are quite certain that no attempt has been made to apply his findings in criminal investigation.

There is no reliable test for estimating accurately the approximate age of dried blood stains, although opinions can be expressed on the degree of fixation of the stains. Glaister[9] testified so in the Ruxton case.

The problem whether a questioned blood stain could be of anthropoid origin has interesting aspects. The forensic textbooks would have us believe that there is a specific test for human blood. No less an authority than Sydney Smith[10] states 'if blood serum has merely to be identified as human as opposed to that of lower animals, the matter is neither difficult or lengthy.' With higher animals it is a little different. Certain research workers tested dried blood stains from apes (chimpanzees), monkeys and lemurs. Gradwohl[11] in 1952 stated that he tested chimpanzee blood against a very potent anti-human sera and obtained reactions identical with that given by human blood. He therefore concluded that anti-human precipitin serum will not differentiate between a garment contaminated with human blood and one contaminated with chimpanzee blood. More recently Shapiro[12] drew attention to the work of Duncan Taylor,[13] who concluded that there is no simple, practical way for laboratory testing which can dis-

tinguish between human blood stains and blood stains from apes and monkeys. From Dr. Taylor's work it is inaccurate to report that a blood stain is of 'human or anthropoid origin'. This puts serologists on the spot because most of us have been doing this for years and getting away with it! However, Dr. Taylor's research finally determined that where the gravity of the case warranted the trouble the specific identity of a particular stain probably could be established. In such a case the appropriate primates would have to be inoculated in order to obtain specific anti-sera for performing the tests. The technique involved would be lengthy and expensive.

Mr. J. Edgar Hoover, Director of the Federal Bureau of Investigation Laboratory at Washington, D.C., in reply to a request for information about the identification of human and primate blood, advised me that they had no material on the subject for distribution. If there is any question about the differentiation of such blood, the F.B.I. Laboratory uses a special turbidimeter, the Photronreflectometer, for this purpose.[14] Dr. Alan Boyden, Director of the Serological Museum of Rutgers University, New Jersey, has done a large amount of research on this method. In a personal communication[15] he has written me that he is familiar with the methods used and the results obtained by Gradwohl and by Duncan Taylor but that their techniques are 50 years old and their results are accordingly out of line with more advanced methods of study. Dr. Boyden stated further: 'Now it is true that some anti-human sera will fail to distinguish between the sera of man and chimpanzee even by refined methods. It is also true that we *can* produce anti-human sera which will distinguish these two by our photoelectric turbidity measurements. But we never have difficulty in distinguishing man from any of the other primates.' At the Fifth International Congress of Blood Transfusion held in Paris, September 1954, Dr. Boyden read a paper on the *'Identification of Unknown Bloods by the Precipitation Reaction Measured With the Libby Photronreflectometer'* (Gemeroy, Boyden, and DeFalco[16]). He stated: 'With this turbidimetric method closely related species that may not be distinguished by other techniques are readily separated. The older or ring test technique measures only the sensitivity of an anti-serum and not its complete reaction capacity. Furthermore it requires knowledge of absolute antigen concentrations if the titer or end point determinations are to be valid. The ring test is much less discriminating than our turbidimetric procedures and of little value for the differentiation of closely related species'.

The inferences which can legitimately be drawn from laboratory data also provide difficult problems in Court, especially for laymen. For example, at a recent murder trial I stated that human blood which demonstrated a positive anti-A factor was identified among skin fragments taken from the deceased's right hand. In all fairness to the accused I could only testify that the blood particles identified *probably* belonged to Group B. (The deceased belonged to group O; the accused belonged to group B.)

Naturally this encouraged the defense attorneys to make me admit that I was not certain of my group findings. In this particular circumstance, of course, no one could be more definite. I was permitted to explain that one can only be certain with the crust slide method of Lattes when one is able to demonstrate both alpha and beta agglutinins. Only positive findings are of significance. In the case just cited, there was always the possibility that the anti-B factor had deteriorated and, if so, the blood would have belonged to a group O individual. The ideal situation is to have sufficient blood to apply both the crust slide method of Lattes and the absorption method.

Summary

An examination of several thousand dried blood stains at the U.S. Army Crime Laboratory in Europe revealed that about 10% of the cases eventually reached Court.

The writer is of the opinion that the demonstration of glycogen in vaginal epithelial cells establishes the stain to be menstrual. Normal surface skin epithelial cells do not store glycogen.

There are no definite blood tests to indicate racial origin or tests to estimate accurately the approximate age of dried blood stains.

Boyden and his co-workers claim that the blood of man can be distinguished from the blood of any other primates by photoelectric turbidity measurements.

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REVIEWS OF BOOKS

Alcohol

Alcohol, Science and Society. Twenty-nine Lectures (Yale Summer School of Alcohol Studies). (Pp. 473. $6.) New Haven: Quarterly Journal of Studies on Alcohol, 1954.

Contents: Foreword. Preface to the Sixth Printing. 1. Introduction to the Curriculum. 2. The Problems of Alcohol. 3. Metabolism of Alcohol. 4. The Concentration of Alcohol in the Blood and Its Significance. 5. The Physiological Effects of Large and Small Amounts of Alcohol. 6. Alcohol and Nutrition: The Diseases of Chronic Alcoholism. 7. Effects of Small Amounts of Alcohol on Psychological Functions. 8. Drinking Mores of the Social Classes. 9. Heredity of the Alcoholic. 10. Children of Alcoholic Parents Raised in Foster Homes. 11. Theories of the Alcoholic Personality. 12. Alcohol and Aggression. 13. The Functions of Alcohol in Primitive Societies. 14. Alcohol and Complex Society. 15. Some Economic Aspects of Inebriety. 16. Excessive Drinking and the Institution of the Family. 17. Alcohol and Pauperism. 18. Alcohol and Traffic. 19. Philosophy of the Temperance Movement. A panel discussion. 20. The Churches and Alcohol. 21. Controlled Consumption of Alcoholic Beverages. 22. Legal Aspects of Prohibition. 23. Analysis of Wet and Dry Propaganda. 24. Penal Handling of Inebriates. 25. Medical Treatment of the Inebriate. 26. The Role of Religious Bodies in the Treatment of Inebriety in the United States. 27. Social Case Work with Inebriates. 28. Pastoral Counseling of Inebriates. 29. The Fellowship of Alcoholics Anonymous.

This volume covers the scope of 29 lectures (with discussions) given at the Yale Summer School of Alcohol Studies. It is in its sixth printing since 1945 and is now the foundation for instruction in a curriculum which attracts some 190 students at each annual session. It could well serve the same purpose in other parts of the world.

New knowledge and development in the past 10 years are summarized in the preface to the sixth printing. Of particular interest is the confirmation by the original work of Bjerver and Goldberg (in Sweden) of the effects of small amounts of alcohol on psychological functions and on the deteriorative effect of 3 or 4 drinks on the skills required in driving.

In cats and rats fundamental work is reported on attempts to find out why, in a neurosis, some individuals resort to acohol so as to become addicted.

The work of Greenberg and Lester illustrates why alcohol, by providing a mild degree of sedation for many drinkers (p. xv) permits them to tolerate a certain amount of stress without severe reaction. This 'may be akin to what many moderate drinkers seek in alcoholic beverages'.

The increasing use of chemical tests of intoxication absolve the innocent as well as convict the guilty; 18 states by 1953 and 464 cities with populations over 10,000 have used chemical tests. The wholly rational basis is adopted that chemical tests furnish needed additional evidence and the emphasis is on blood tests. This sound approach can certainly be endorsed, as the validity of the inferences to be drawn from the results obtained by the use of breath or urine is disputed too seriously in scientific circles to justify the employment of breath and urine tests by themselves, if an arbitrary attitude of this problem is to be avoided.

The volume also deals with two schools of thought about the etiology of alcoholism. The one school regards it as the manifestation of a neurosis, whereas the other regards it as a biochemical difficulty genetically determined. The evidence for the latter view is somewhat slender, but it is typical of the important issues with which this volume is concerned, that the matter is ventilated adequately.

The social worker, the anthropologist, the physiologist and the clinician will find in this volume a considerable storehouse of useful information. There are extremely interesting and instructive discussions and the treatment of alcoholism (psychotherapy, antabus, the conditioned reflex aversion, hormonal adjuncts, etc.), as well as the function of alcohol in primitive societies and the drinking customs in different social strata. The importance of diet in the development of the so-called alcoholic cirrhosis of the liver is also reviewed.

This excellent contribution to the understanding and the treatment of one of our most important social problems concludes appropriately enough with an informative survey of Alcoholics Anonymous.

Smith's and Fiddes: Forensic Medicine

Forensic Medicine. By Sir Sydney Smith, *C.B.E.*, LL.D. and Frederick Smith Fiddes, *O.B.E.*, M.D. (Pp. 623+Index. With 173 illustrations. 40s.) 10th ed., 1955. London: J. & A., Churchill Ltd.

Contents: 1. Legal Procedure in England, Scotland and Ireland. 2. The Signs of Death and Subsequent Phenomena. 3. Sudden Death from Natural Causes. 4. Post-mortem Examination of the Body. Exhumations. Embalming. Death Certification. Cremation. 5. Identification. 6. Wounds. 7. Injuries in Various Parts of the Body. 8. Self-Inflicted Wounds and Fabrications. 9. Wounds from Firearms. 10. Differential Diagnosis in States of Insensibility. 11. Examination of Blood Stains. 12. Injuries from Burns and Scalds. Corrosive Fluids. Spontaneous Combustion. Injuries from Electric Currents, from Lightning and Radiation. Death from Heat. Cold. Starvation and Neglect. 13. Violent Death from Asphyxia. 14. Asphyxia from Breathing Irrespirable Gases. 15. Impotence and Sterility. Artificial Insemination. 16. Rape and Indecent Offences. 17. Pregnancy and Delivery. Unusual forms of Pregnancy. Birth in its Civil Aspects. 18. Abortion. Development of Foetus. 19. Infanticide or Child Murder. 20. Ethics and Law in the Conduct of Medical Practice. 21. Insanity. Insanity and Responsibility. Lunacy Certification. 22. Toxicology. 23. Corrosive Poisons. 24. Metallic Poisons. 25. Common Hypnotics, Antipyretics and Anaesthetics. 26. Vegetable Poisons. 27. Miscellaneous Poisons. 28. Food Poisoning. Cadaveric Alkaloids. Appendices: 1. Systematic Analysis of the Viscera for Poisons. 2. Preservation of Specimens. 3. Weights and Measurements of Organs. Composition of Normal Blood and Normal Urine. 4. Forensic Medicine in the East. 5. Fees and Allowances for Medical Witnesses. Index.

The 10th edition of this well-known and standard work, relied on by many generations of students and practitioners, has been issued in an entirely new format. The more elegant proportions of the new volume have made possible a reduction in the actual number of pages thus making the book pleasant to handle as well as instructive to read.

The authors point out that the effect of the Coroners' Rules of 1953 have stimulated a more wide-spread interest in forensic pathology amongst those involved in the more purely pathological aspects of this work. 'There are, however, many parts of the world where it is impracticable to enforce any such rules, and there are, moreover, many aspects of the subject which still primarily concern the practitioner.

'He is frequently the first, and from the practical point of view the most important, medical witness in cases of assault, rape, or homicide, and in many civil actions his evidence is of prime importance.' This quotation makes it clear why the practitioner who aims at retaining his competence needs to equip himself for the wide variety of cases he will encounter in the course of his clinical practice.

Forensic Medicine achieves the dual objective of being not only an adequate manual for the undergraduate student, but also a comprehensive source book and work of reference for the qualified practitioner whether his career is in the clinical or in the more specialized forensic field.

Synopsis of Forensic Medicine

A Synopsis of Forensic Medicine and Toxicology. By E. W. Caryl Thomas, M.D., B.Sc. (Lond.), D.P.H., Barrister-at-Law. (Pp. 176 + Index. 12s. 6d.) 3rd ed., 1954. Bristol: John Wright & Sons Ltd., 1954.

Contents: 1. Legal Position and Responsibilities of the Medical Man. 2. Medical Evidence. 3. Signs of Death and Phenomena which follow Death. 4. Medico-Legal Aspect of Identification. Examination of the Dead. Exhumation and Embalming. 5. Modes of Dying. 6. Death from Special Causes. 7. Death from Special Causes (continued). 8. Examination and Recognition of Blood Stains. 9. Sexual Matters and Pregnancy. 10. Abortion, Birth, Infanticide. Stillborn. 11. Insanity. Mental Deficiency. Drunkenness in its Legal Relations. 12. Insurance. 13. Toxicology. 14. Corrosive and Irritant Poisons. 15. Narcotic and Other Poisons.

In the course of two decades this little volume now sees its third edition, in which the author states in a new preface: 'Forensic Medicine and Toxicology are subjects which change little with the passing of time.' This is a most inaccurate generalization and in conflict with the extensive revisions required in every new edition of standard works on the subject published in the United Kingdom and the United States of America. More recently Keith Simpson's *Modern Trends in Forensic Medicine* has illustrated the many important advances made and a careful study of which would undoubtedly be of profit to the next edition of Dr. Thomas' *Synopsis*. There is, in the light of modern knowledge, no justification for perpetuating such views as that coma and asphyxia are pathological entities recognizable at autopsy (p. 63); that coagulation of the blood is delayed in asphyxia (p. 41); that Tardieu's spots are more common in rapid deaths and are of pathognomonic significance in suffocation and asphyxia (pp. 64, 89).

The author, however, makes the valid point on p. 82 when he points out that, although there is nothing characteristic of the autopsy appearances in death from cold, the hue of the blood throughout the body is arterial. This is a sound observation. The effects of refrigeration on the colour of the blood deserve wider recognition and appreciation.

It is remarkable that in a discussion of the blood groups no mention is made of the medico-legally important Rh factor. However, the changes brought about by the National Health Service Act and various other legislative amendments appear to have been incorporated adequately.

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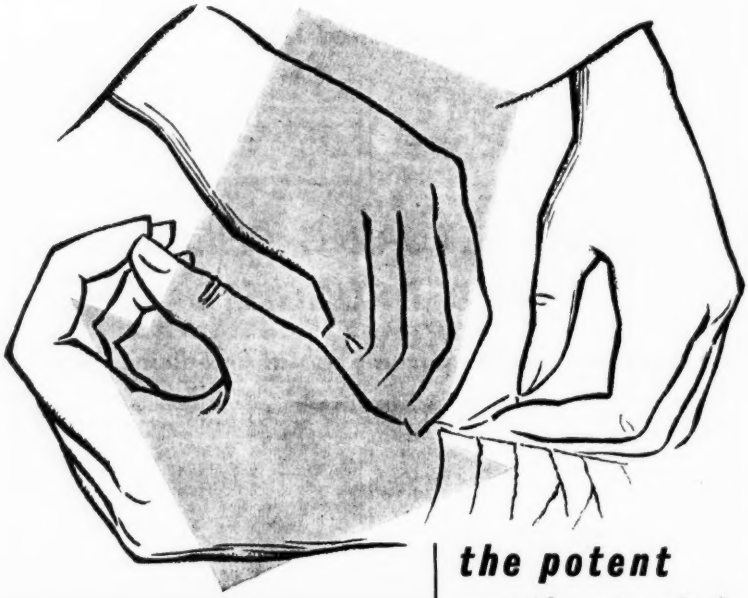

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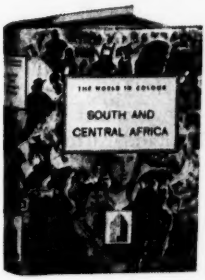

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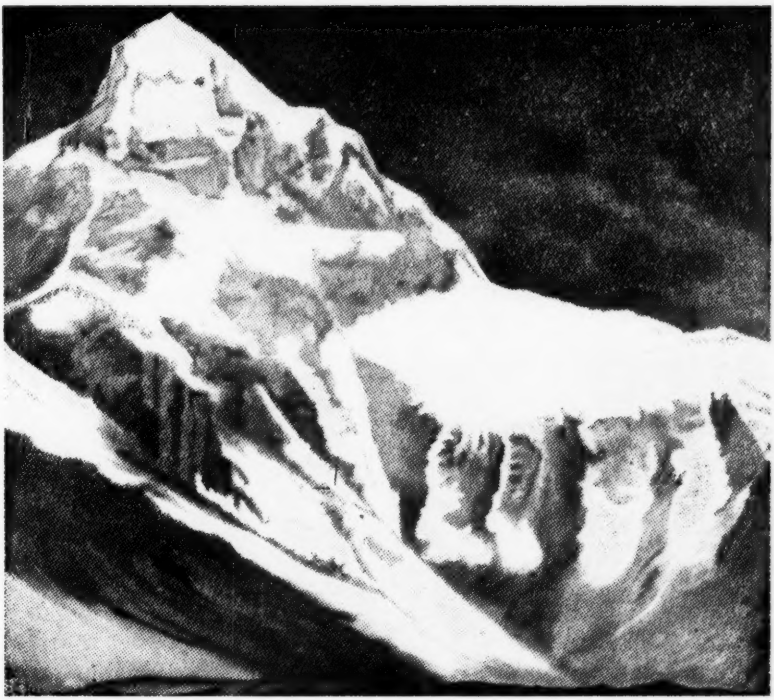

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